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OBSERVATIONS ON 117 PATIENTS OPERATED ON FOR CONGENITAL PULMONARY STENOSIS

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A SUCCESSFUL operation for the relief of congenital pulmonary stenosis was reported by Blalock and Taussig[1] in 1945. The success of the operation depended upon increasing the flow of blood to the lungs. This was accomplished by making an end to side anastomosis between one of the branches of the aortic arch, usually the subclavian artery, and a pulmonary artery. In 1946, Potts, Smith and Gibson[2] reported a modification of the above technic whereby a side to side anastomosis between the aorta and a pulmonary artery was done. This was made possible by the invention of a clamp which encircled the aorta and merely pinched off a lip, thus allowing blood to flow through the aorta while the anastomosis was carried out.

Since Sept. 13, 1946, 117 patients have been operated on for congenital stenosis of the pulmonary artery at the Children's Memorial Hospital. The Potts-Smith technic was used in 104 cases, the Blalock technic in one. Exploration alone was done in 12 patients. Obviously, at the present time the long term value of this operation cannot be assessed. Yet the results to date have been so heartening that a progress report is worth while.

Congenital stenosis of the pulmonary artery rarely exists alone. It occurs most frequently in conjunction with a defect of the interventricular septum, dextroposition of the aorta and hypertrophy of the right ventricle. This syndrome is known as the tetralogy of Fallot.

Diagnosis in the typical case of tetralogy of Fallot is usually easy. The patient gives a history of cyanosis beginning during the first year of life. He is a poor eater and slow in weight gain and growth. He is irritable and fussy, a child who gets little pleasure out of life. His ability to exercise is markedly limited, limited in walking, for example, to only a few hundred feet. He becomes dyspneic easily and assumes a characteristic

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squatting position, as a rule, until his distress subsides. Upper respiratory infections are frequent. Hospitalization for oxygen therapy is occasionally necessary. Repeated fainting spells or episodes of paroxysmal dyspnea are common. Convulsions and hemiplegia are not infrequently seen.

The child, on examination, is thin and underdeveloped with flabby musculature and

TABLE I

HISTORY AND PHYSICAL EXAMINATION

	Present	Absent	Too Small	Not Recorded
Dyspnea	117	0	—	—
Physical retardation	75	37	3	2
Paroxysmal dyspnea	55	55	—	7
Thrill	52	64	—	1
Fainting	47	68	—	2
Convulsions	12	104	—	1
Hemiplegia	5	112	—	—

	Normal	Retarded	Fair	Poor
Mental development	101	16	—	—
Build	23	—	37	57

	Normal	Marked	Moderate	Mild	Absent	Not Recorded
Proclivity to infections	65	48	—	—	—	4
Cyanosis	—	52	30	35	0	—
Clubbing	—	29	42	41	5	—
Suffusion of conjunctivae	—	14	44	45	6	8

	Normal	Enlarged	Slightly enlarged
Heart size	102	11	4
Liver	102	15	—

	At Birth	Neonatal	Later	
Appearance of cyanosis	36	15	66	(range, 1–60 mo.: average 8 mo.)

	Yes	No	Not walking	Not recorded
Squatting	64	6	27	20

	Clear, not accentuated	Split	Snapping	Not recorded
P-2	68	1	8	40

Additional malformation	7
Family history, congenital heart disease	5
History of rubella in mother during pregnancy	0
Other anomalies	1

marked cyanosis especially around the lips, mucous membranes, tips of the fingers and toes. There is suffusion of the conjunctivae. The fingers and toes are clubbed. The heart is usually not enlarged. There is often a systolic thrill, felt best near the sternum at about the third left intercostal space. In this region there is a systolic murmur. The second pulmonary sound is usually rather quiet but clear. The blood pressure is often difficult to obtain and pulse pressure is narrow. The liver may be slightly enlarged; the spleen is not felt. There is a polycythemia of varying degree. The A-P roentgenogram reveals a heart that is boot-shaped, with a concavity in the region of the pulmonary conus, and avascular lung fields. In the left anterior oblique view, an abnormally clear pulmonary window is seen under the fluoroscope. The electrocardiogram shows axis deviation to the right. Such is the typical story of the patient with the tetralogy of Fallot.

One further point, however, must be considered before the diagnostic workup is complete. It must be determined whether the arch of the aorta lies on the left or on the right side. To accomplish the side to side anastomosis of the aorta to a pulmonary artery by the Potts-Smith technic, the chest must be entered on the side on which the arch lies. In the tetralogy of Fallot the aortic arch descends on the right side in approximately 20 to 25% of cases. In this series of 108 cases of tetralogy there were 28 patients with right aortic arch.

Usually the diagnosis of the correct position of the arch is easy. With a swallow of barium, indentation of the esophagus by the aorta can be detected in the great majority of cases. With a left arch the esophagus is indented on the left. With a right arch it is indented on the right. In a few cases it is extremely difficult to determine its position. When the position is doubtful, the arch can usually be assumed to be on the right.

Some of the variations from the typical picture described should be discussed. From the standpoint of history and general physical findings this series of patients adheres closely to the typical picture. Table I summarizes the salient points.

Evaluation of the murmurs heard over the heart constitutes one of the most important features of the physical examination and is worthy of emphasis since it offers valuable information both as to diagnosis and prognosis. A murmur was present in 113 patients. In the vast majority the murmur was purely systolic in time, maximal in or near the third intercostal space close to the sternum, rather harsh in quality and usually heard throughout systole. It had the quality of a "squirt" and did not resemble the blowing murmur characteristic of acquired heart disease. In no case was it loudest over the apex.

Four patients had no murmur. In addition, seven patients had atypical murmurs in that the murmurs had diastolic components or were abnormally located in their maximal intensity. Table II summarizes the auscultatory findings.

What causes the murmur in the tetralogy of Fallot? Is it due to the stenosis of the pulmonary orifice, to the defect in the ventricular septum, or to both? The theory here is that it is due to the pulmonic stenosis. With an aorta that overrides both ventricles and lies immediately above a septal defect, it would seem that most of the blood leaving the ventricles would go directly into the aorta and not into the other ventricle. This should cause no murmur. On the other hand, blood passing through a stenosed pulmonary tract into a relatively dilated pulmonary artery would far better explain the murmur.

This theory is borne out by the findings. Of the four children who had no murmur, the first (L.D., Case 16) underwent operation. A small pulmonary artery was found which was successfully anastomosed to the aorta with excellent results. The next child without

a murmur (S.W., Case 41) died following surgery. At postmortem examination, atresia of the pulmonary artery was found. The blood supply to the lungs was solely dependent on two bronchial arteries. In this case the aorta overrode both ventricles and there was a sizeable septal defect. Yet there was no murmur. The third (B.K., Case 37) was successfully operated upon and a left pulmonary artery no larger than a lead pencil found. It was noted at operation that there was no thrill over the base of the heart. The absence of a thrill at operation has been noted in all those cases of pulmonary atresia seen at post mortem. The fourth (G.A., Case 85) died during the operation. At post mortem an atresia of the pulmonary artery at the base of the heart was found. The only blood to the lungs came through a patent ductus arteriosus that was almost completely obliterated.

TABLE II

SUMMARY OF MURMURS HEARD

Location (Maximal Intensity)	
Second to fourth left intercostal space	107
Midline manubrium	1
First and second right intercostal space	3
Second left and right intercostal space	1
Back	1
None	4
	117
Quality	
Harsh systolic	106
Functional-sounding systolic	2
Humming-top	2
Systolic with diastolic	3
None	4
	117

A careful history elicited the information that this child had done well until just a few months prior to operation. During those few months he had failed rapidly, ceased to walk, had frequent episodes of severe paroxysmal dyspnea and fainting, refused food, and generally showed marked increase in cardiac symptoms. This history fits in well with the findings at necropsy, for one would suspect that the ductus had rather recently started to close, and that it would have been completely obliterated in a short time. It is believed that this child died on the operating table because tension put on the left pulmonary artery to bring it up to the aorta for anastomosis was sufficient to shut off what little blood was passing through the ductus.

Thus two of the four patients without murmurs were proven to have pulmonary atresia. A third patient was believed to have an atresia because of the lack of the characteristic thrill felt over the base of the heart at the time of surgery. Of the four without murmurs only two could be helped; the others died following exploration. The absence of murmurs, therefore, seems to be of prognostic significance. However, it should be pointed out that a pulmonary artery which is atretic at its source may be amply patent distally for the purpose of anastomosis.

Seven patients had murmurs that were definitely atypical. In one of these (J.M., Case 60) there was a long systolic and a short, soft diastolic murmur heard in the second intercostal space equally well to the right and left of the sternum. Anastomosis could not be accomplished because the right pulmonary artery was only one mm. in diameter. Three hours following operation death occurred due to anoxia. At autopsy, atresia of the main pulmonary artery was found. The aortic arch was on the right side. From the aorta arose a bronchial artery which passed between the esophagus and trachea and entered the left lung. It was felt that this kinked and tortuous vessel was the cause of the murmur. In a second child (V.S., Case 49) with a humming-top murmur heard in the first and second right intercostal spaces, the anastomosis could not be done because the pulmonary artery was absent. At operation it was noted that there was a tortuous bronchial artery supplying the right lung. It is an interesting sidelight that this child was improved subjectively and objectively by operation, despite the fact that no anastomosis was done. This might be explained by theorizing that a better flow of blood to the right lung was created when the bronchial artery was dissected free and allowed to follow a straighter course. Whether the child is still better off than before operation is not known. A third child (C.J., Case 100) had a loud, harsh, humming-top murmur heard throughout the chest, perhaps loudest at the right base posteriorly. At operation, no trace of a pulmonary artery was found. From the aorta, which was large, arose several bronchial arteries which supplied both lungs. No anastomosis could be done. The child recovered following operation and seemed to be somewhat benefited by the dissection and freeing of the bronchial arteries. A fourth child (R.B., Case 45) had a systolic and diastolic murmur in the second left intercostal space. Anastomosis was accomplished and the child was greatly benefited. In this patient no pulsations were felt over the pulmonary artery. There was a continuous thrill over the base of the heart, though there was no patent ductus. The cause of the thrill is not known. The other three patients (S.H., Case 24, S.S., Case 50, T.R., Case 59) with atypical murmurs did well following operation. The pulmonary arteries in all cases were small, but anastomoses were successfully accomplished and the results were good.

Experience to date suggests that absence of a murmur indicates pulmonary atresia, and that the presence of atypical murmurs indicates large bronchial arteries which supply the greater portion of blood to the lungs. Of the 11 patients with absent or atypical murmurs, anastomosis could not be done in four because of an absent pulmonary artery. Another died because of interference with the only apparent flow of blood to the lungs, namely, that through a small patent ductus. Five of the 11 cases resulted in failure. In the presence of these abnormal clinical findings, therefore, surgery carries a decidedly greater risk than in the typical case. Yet exploration should be undertaken in the hope that a pulmonary artery large enough to permit an anastomosis may be found.

Roentgenographic and Fluoroscopic Findings

In the normal heart the right ventricle rests on the diaphragm and is anterior; the left ventricle is posterior and makes up the lower left border of the heart when viewed in the anteroposterior position. In the tetralogy of Fallot the left heart is small but the right ventricle is relatively large. In addition, there is stenosis of the conus portion of the right ventricle and a small pulmonary artery. Hence one sees a heart that sits high on the diaphragm and seems to lie transversely rather than extending downward below the dome of the diaphragm. The left border of the heart, just beneath the arch of the

aorta, is concave, for the conus portion of the right ventricle and the pulmonary artery are small. Typically, the impression received is that of a boot resting on the diaphragm with the toe extending straight out to the left. The heel is made up of the enlarged right auricle and possibly the right ventricle (see Fig. 1).

In the left anterior oblique view the heart extends farther forward than normally because of the enlarged right ventricle. The arch of the aorta can occasionally be seen. Under this there is a clear space, a space normally filled by a pulsating pulmonary artery. This is the pulmonary window (Fig. 3). In the right anterior oblique position the right ventricle extends well forward to the sternal wall. Instead of sloping gently in a posterior and cephalad direction, there is a clearcut shelf caused by the small conus and pulmonary artery.

There are many variations from this typical picture. In our series the size of the pulmonary artery has varied from being atretic to being a good deal larger than normal. The artery may be atretic at its source, but large and thin-walled distally. There may be only a slight conus stenosis but a small pulmonary artery. Atresia may involve the conus portion, the pulmonary valve, the base of the pulmonary artery, or the entire artery. It is impossible to be sure of the exact status of the pulmonary circulation without direct visualization at operation. However, the X-ray silhouette offers definite aid.

An atresia of the pulmonary artery for the greater part of its length throws no shadow on X-ray and hence there is a marked concavity in the region of the pulmonary artery and a clear pulmonary window. Of those proved pulmonary atresias, all had a typical if not an exaggerated boot shape and all had a clear pulmonary window.

If there is a pulmonary artery present of relatively normal size and carrying some blood, it may usually be seen in the hilar region. When the main pulmonary arteries can be seen, the heart, as a rule, appears less typically boot-shaped with the left upper salient likely to appear straight rather than concave. In such cases the pulmonary window is not particularly clear.

The origin of the aorta causes variations in the X-ray silhouette. Typically, the aorta overrides both ventricles. The degree of overriding, however, varies a great deal. If the aorta almost completely overrides the right ventricle, it arises from a point anterior to its customary position. This widens the pulmonary window in the left anterior oblique position. On the other hand, if the aorta arises almost completely from the left ventricle, its origin is moved posteriorly; hence, the pulmonary window is rather narrow.

In general, there seems to be some correlation between the X-ray silhouette of the heart and the severity of the patient's symptoms. As has been stated, all patients who have had a proved atresia of the pulmonary artery have had a typical if not exaggerated boot-shaped heart. These patients have usually been severely incapacitated. It seems definite that the more marked the symptoms, the more typical the boot and the clearer the pulmonary window. The converse of this should be true and it follows fairly closely.

Roentgenographic and fluoroscopic studies must not stop with an analysis of the cardiac silhouette. The lung fields must be scrutinized closely for evidence of decreased circulation. Under fluoroscopy the pulmonary arteries must be examined for pulsations. Pulsations of the pulmonary arteries mean that an ample amount of blood is passing to the lungs. Such pulsations contraindicate operation. One such patient (K.G., Case 79) has been operated on at the insistence of the family, despite the fact that pulmonary pulsations were thought to be present. At operation a large pulmonary artery pulsating as markedly as did the aorta was found. No anastomosis was done since it was obvious

that the lungs were receiving enough blood. The diagnosis is still in doubt, though it is believed that the child had a transposition of the great vessels. The postoperative course was uneventful.

A superficial glance at the roentgenogram often seems to indicate normal or increased vascularity. A closer look will demonstrate that such markings are very fine. No vessels are seen tangentially. Difficulty arises when the patient has had repeated pulmonary infections with scarring, but such scarring must be differentiated from vascular markings. The differentiation is fundamental, for there is no more important diagnostic criterion than the vascularity of the lung fields.

Tricuspid Atresia

Congenital stenosis of the pulmonary arteries occurs in conjunction with another syndrome which differs anatomically from the tetralogy of Fallot. In this syndrome tricuspid atresia would seem to be the primary lesion. Blood is unable to pass from the right auricle to the right ventricle and must be shunted through an open foramen ovale or an interauricular septal defect into the left auricle. From the left auricle the blood passes into the left ventricle, whence a portion passes through an interventricular septal defect into a diminutive right ventricle and out through a stenotic pulmonary artery to the lungs. Here again there is a venous-arterial shunt and an inadequate flow of blood to the lungs. The clinical picture is similar to that of the tetralogy of Fallot. It varies, however, in two important respects. Roentgenographic and fluoroscopic studies reveal the relatively large left ventricle and small right ventricle. In the A-P view there is a gentle rounding of the left cardiac salient and the heart appears to dip slightly below the diaphragm (Fig. 2). In the left anterior oblique view, the heart projects posteriorly toward the spine and fails to project anteriorly into the retrosternal space. The pulmonary window is clear (Fig. 4).

Because the left ventricle is carrying the greater part of the burden, one would expect to find left axis deviation in the electrocardiogram, and such is the case. In fact, tricuspid atresia is practically the only congenital heart lesion in patients with cyanosis in which left axis deviation occurs.

In this series there were six patients with tricuspid atresia. Of these, four were found to have small pulmonary arteries, with faint pulsations present (T.D., Case 19, J.C., Case 21, H.Z. Case 29, N.B., Case 108). In these four an anastomosis was completed with recovery and marked improvement of symptoms. The fifth patient (B.V.R., Case 56) had no pulsation present in the pulmonary arteries. There was a systolic murmur present, thought to be due to an interauricular septal defect. An anastomosis was successfully completed and the child did well following operation. The sixth child (D.L., Case 28) died following a satisfactory anastomosis, with symptoms suggesting cerebral hemorrhage. No post mortem was granted, so the diagnosis of tricuspid atresia could not be proven. Thus a patent pulmonary artery was found and anastomosis was possible in all six of the patients with tricuspid atresia.

Pulmonary Valve Stenosis

A third congenital heart condition simulating the tetralogy of Fallot is that of pulmonary valve stenosis with a patent foramen ovale. There was one such patient diagnosed at postmortem examination and not preoperatively. This patient (J.L., Case 88) had a marked pulmonary valve stenosis and marked right ventricular hypertrophy. Beyond the pulmonary valve there was a large, thin-walled, hypoplastic artery. The tricuspid valve

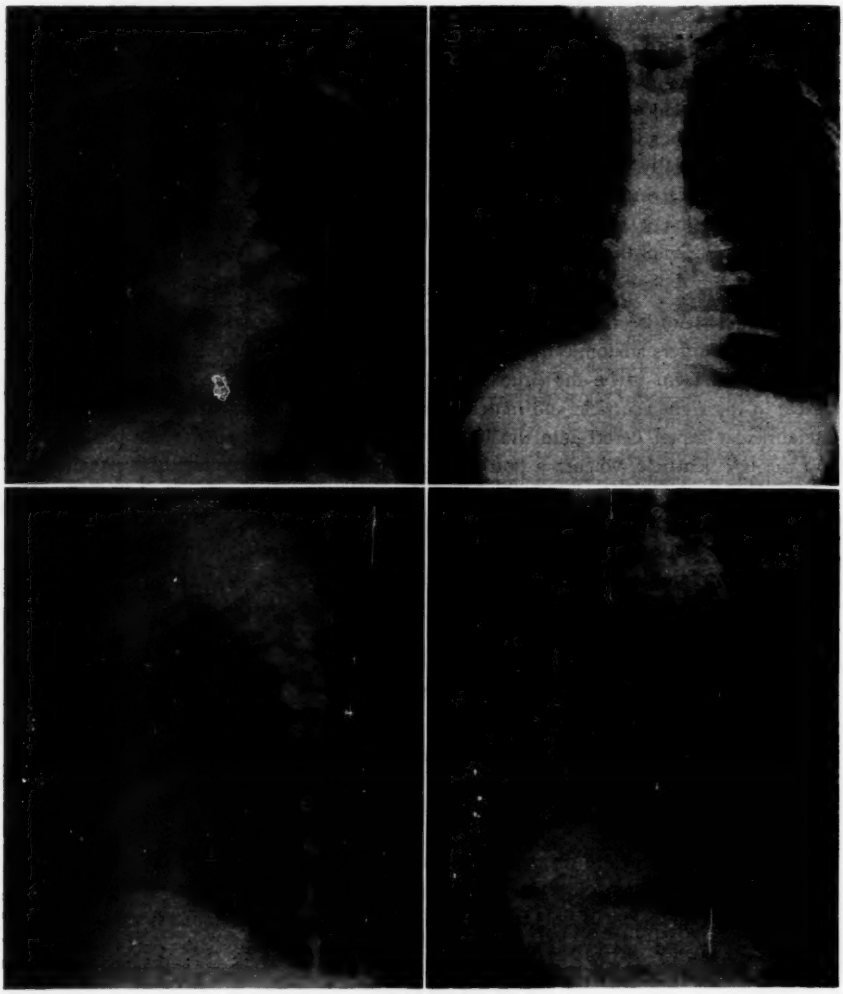

FIG. 1. Tetralogy of Fallot in A-P Position.
FIG. 2. Tricuspid Atresia in A-P Position.
FIG. 3. Tetralogy of Fallot in Left Anterior Oblique Position.
FIG. 4. Tricuspid Atresia in Left Anterior Oblique Position.

showed evidence of thickening and insufficiency. The foramen ovale was functionally patent. On roentgen examination the heart was enlarged, there was a slight concavity where the conus portion of the right ventricle should be and, just above this, there was a convexity, the pulmonary artery. The pulmonary window was not clear.

EXPLORATORY OPERATIONS

The 117 cases reported in this paper include 12 patients who were explored but in whom an anastomosis was not done. Of these 12, anastomosis could not be performed

in eight of them because of an atretic pulmonary artery. In addition, one patient (G.M., Case 4) was explored and anastomosis was deemed unwise, because high pressure in the pulmonary artery indicated that the patient probably had an Eisenmenger's syndrome rather than the tetralogy of Fallot. In the patient previously mentioned (K.G., Case 79) with a probable transposition of the great vessels, anastomosis was not attempted. Another patient, previously mentioned (G.A., Case 85), expired before an anastomosis could be accomplished, probably because of interference with the circulation to the lungs

TABLE III

EXPLORATORY OPERATIONS

Name	Age yr.	Summary
1. G.M. # 4	6	Large pulmonary artery with what seemed to be normal pressure was discovered. It was felt that the patient had an Eisenmenger's syndrome. Recovered.
2. K.F. # 10	1	No pulmonary artery found; no anastomosis. Recovered.
3. G.R. # 15	3	No pulmonary artery found; no anastomosis. Died at end of operation. Cause of death—cerebral anoxia.
4. M.T. # 25	2	Pulmonary artery too small; no anastomosis. Died 35 min. after operation. Cause of death—cerebral anoxia.
5. S.W. # 41	8	No pulmonary artery found; no anastomosis. Died 58 hrs. postoperatively. Cause of death—cerebral anoxia and bilateral bronchopneumonia.
6. V.S. # 49	11	Pulmonary artery too small; no anastomosis. Large bronchial arteries present. Recovered; somewhat benefited.
7. T.M. # 60	7	Pulmonary artery too small; no anastomosis. Died 3 hrs. postoperatively. Cause of death—cerebral anoxia. Large bronchial arteries found.
8. K.G. # 79	1	Large, markedly pulsating pulmonary artery found; suspected transposition of great vessels; no anastomosis. Recovered.
9. G.A. # 85	3	Small pulmonary artery found. Died before anastomosis could be done because of accidental constriction of only source of blood to lungs, a patent ductus. Cause of death—cerebral anoxia.
10. C.J. #100	6	No pulmonary artery found; no anastomosis. Large bronchial arteries found. Recovered.
11. R.F. #111	12	Pulmonary artery only 1 mm. in diameter; no anastomosis. Recovered.
12. R.F. #114	5	Pulmonary artery large enough but technical difficulties too great; no anastomosis. Died 6 hrs. postoperatively. Cause of death—cerebral anoxia.
Total cases 12 Total deaths 6		

Note: The two cases operated upon a second time because of incorrect diagnosis of the location of the aortic arch are not included in this list of exploratory operations.

through a small patent ductus arteriosus. The twelfth patient (R.F., Case 114) presented apparently insurmountable technical difficulties. Arising from a right aortic arch, at a point at which a Potts-Smith anastomosis would be done, was a large bronchial artery carrying blood to the right lung. When this vessel was occluded, the heart ceased beating. In order to bring down the right subclavian artery and anastomose it to the right pulmonary artery, pressure had to be put on an enormous azygous vein and this caused the heart to stop. The lung could not be completely collapsed without the heart stopping. There seemed no way to overcome these difficulties. The child was returned to his room where he died a few hours later due to severe anoxia.

Of these 12 children, six died, a mortality rate of 50%. It is obvious from these figures that an exploratory operation carries with it a far greater risk than an operation with a successful anastomosis. Surgery must not be undertaken too lightly if the diagnosis is in doubt. The possibility of not being able to accomplish the anastomosis and the consequent increase in the risk must be carefully explained to the parents before operation is undertaken. Table III summarizes the results in the explored group.

Operative Results

Among the 105 patients in whom an aortic-pulmonary anastomosis was done there were 10 fatalities, a mortality rate of 9.5% The over-all mortality rate for the series is 13.8%. A breakdown according to age grouping is of special interest (see Table IV).

TABLE IV

Mortality Rates

Age	Cases	Deaths	Percentage
	Aortic Pulmonary Anastomosis		
0–1	9	1	11.0%
1–2	15	3	20.0%
2–3	13	2	15.4%
3–8	48	2	4.1%
8–16	20	2	10.0%
Total	105	10	9.5%
	Exploratory Operations		
0–16	12	6	50.0%
Total	117	16	13.8%

From this analysis it would seem that the safest age for operation is between the ages of three and eight, and that infancy is the most dangerous. These figures, however, are open to question because the infants operated upon were so severely handicapped that survival could not be hoped for without surgery.

Table V summarizes the causes of death in our series of 117 patients.

There have been six cerebral vascular accidents in our series. All occurred during or immediately after surgery. Four of these patients died; the other two recovered, one with moderate spasticity of the right side which is gradually clearing, the other with

minimal weakness of the right side. In addition, there was one case of severe cerebral anoxia with coma for four days, but without residual neurologic findings.

Two children died because of avoidable surgical complications. The first developed a tension pneumothorax immediately after closure of the chest. Postmortem examination revealed an old tuberculous lesion at the apex of the left lung which, after the adhesions over the pleura were broken to collapse the lung, formed a bronchopleural fistula. The second child exsanguinated from a leaking intercostal artery during the first 24 hours after operation. In no case has the anastomosis leaked or torn.

All but one of the patients who died came to autopsy. The one not studied was believed to have a tricuspid atresia and to have died following a cerebral vascular accident. Of the 15 examined, 14 had a typical tetralogy of Fallot with either stenosis or atresia of the pulmonary artery. The fifteenth patient had a valvular pulmonary stenosis with a patent foramen ovale.

The results among the patients successfully operated upon have to date been gen-

TABLE V

CAUSES OF DEATH

Cause of Death	Anastomosis	Exploratory Operation
Cerebral anoxia	1	5
Cerebral accident	4	0
Pneumonia	1	1
Endarteritis, sepsis	1	0
Pressure pneumothorax	1	0
Exsanguination—intercostal artery	1	0
Thrombosis anastomotic site, saddle embolism, anoxia	1	0
Total	10	6

erally satisfactory. However, some of the patients have developed complications to which attention should be called. Patients with a right aortic arch have presented certain problems not seen in those with a left aortic arch. As has been said, the aortic arch was on the right in 28 of our 108 patients with a tetralogy of Fallot (26%). Two errors were made in the series, one through failure to study the roentgenograms closely and the other through faulty interpretation. Both these patients were explored and closed when the mistake was discovered, to be re-operated upon a few months later. Surgery is more difficult when the arch is on the right. This is because the bronchus tends to separate the aorta and the pulmonary artery on the right, and a good deal of tension must be put on the vessels to pull them together. In addition, on the right the pulmonary artery lies at right angles to the aorta instead of side by side with it. One patient (D.P., Case 20) has developed a chronic right middle lobe infection, apparently due to a sharply angulated bronchus as seen on bronchoscopic examination. This angulation may have been due to stress caused by the anastomosis. Another patient (A.P., Case 83) developed thrombosis at the site of the anastomosis. Part of this thrombus dislodged, causing a saddle embolism. An embolectomy so soon after the first operation proved too great an ordeal and the child expired. A third patient (P.P., Case 103) left the operating room with a low blood pressure which persisted for 16 hours. Thrombosis occurred at the

anastomotic site and the child failed to show any improvement during her hospital stay. Follow-up visits, however, have shown rather marked subjective and objective improvement, despite the absence of the characteristic postoperative humming-top murmur. This suggests that the anastomosis has partially recanalized. Several of the older children have not developed the typical humming-top murmur for a considerable time after operation, and have been slower to show improvement in color and exercise tolerance. The infants with right aortic arches, in contrast to the older children, seem to tolerate surgery well and the results have been favorable.

Another postoperative complication which has caused some concern is excessive cardiac enlargement with cardiac failure. A few of the patients have shown excessive cardiac enlargement. Two have shown heart failure. In both instances too great a strain has been put on the left heart and there has been gradual and progressive cardiac enlargement and, finally, evidence of decompensation. All patients may be expected to show some cardiac enlargement following surgery, but that enlargement should be kept to a minimum. The problem is to keep the enlargement down and, at the same time, increase the flow of blood to the lungs sufficiently to overcome the patient's handicap. Among other things, this depends upon the size of the anastomosis. In the first few patients operated upon, the length of the incision in the aorta was 5/16 to 6/16 of an inch. At the present time the authors believe that an incision of 4/16 of an inch is preferable. The shorter incision seems to offer a satisfactory relief from cyanosis and should place less strain upon the left heart.

In general, most of the patients have shown a truly remarkable change. Cyanosis and dyspnea have been relieved. Appetite has improved. Dispositions have undergone a true metamorphosis. The ultimate prognosis in patients in whom an aortic-pulmonary anastomosis has been performed is unknown. The immediate results have fully justified the procedure and made this operation eminently worth while.

Summary

Operations were performed on 117 patients with congenital pulmonary stenosis or atresia.

Diagnosis in the patient with a typical tetralogy of Fallot is not difficult. Variations from this typical picture, noted on physical examination, roentgenogram and fluoroscopy, are discussed.

Six patients with tricuspid atresia are reviewed with particular reference to differential diagnosis.

One patient with pulmonary valve stenosis and a patent foramen ovale is presented.

An aortic-pulmonary anastomosis was accomplished in 105 patients with 10 deaths, a mortality rate of 9.5%. Twelve patients were explored with a mortality of 50%. The over-all mortality was 13.8%. The causes of death are reviewed.

Results have been slightly less satisfactory in older patients with a right aortic arch than in those patients with a left aortic arch.

Excessive cardiac enlargement has occurred in a few instances.

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SPANISH ABSTRACT

Observaciones en 117 Pacientes Operados de Estenosis Congénita

Se han operado en el Children's Memorial Hospital 117 pacientes con estenosis congénita o con atresia de la arteria pulmonar. Se llevó a cabo una anastomosis aortica-pulmonar en 105 pacientes habiendo habido 10 muertes, una mortalidad de 9.5%. Doce pacientes fueron examinados con una mortalidad de 50%. La mortalidad total fué 13.8%. La causa de muerte más común fué la anoxia cerebral. Complicaciones quirúrgicas evitables causaron dos muertes.

Habían 108 pacientes con tetralogía de Fallot, seis pacientes con atresia tricúspide, uno con un síndrome de Eisenmenger, uno con una transposición de los grandes vasos y uno con una estenosis valvular pulmónica pura. En pacientes atípicos el murmullo puede estar ausente o ser diferente en calidad o situación. En el primer caso significa atresia pulmonar, en el último significa grandes arterias bronquiales como la fuente principal de sangre a los pulmones. Tales descubrimientos atípicos justifican una prognosis cautelosa.

La atresia tricúspide difiere de la tetralogíca de Fallot solamente en dos respectos: (1) Prueba del ensachamiento ventricular izquierdo y una ausencia o un ventrículo derecho pequeño en los rayos-X y fluoroscopía. (2) Desviación del axis izquierdo en lugar de desviación del axis derecho en el electrocardiograma. Los resultados quirúrgicos son igualmente buenos.

707 *Fullerton Ave.*

SOCIAL ADJUSTMENT OF SIX PATIENTS WITH HEMOPHILIA PRIOR TO AND DURING PROPHYLACTIC TREATMENT

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INTRODUCTION

Hemophilia is a serious hereditary disease due to retarded coagulation of the blood. The course of most hemophiliac patients shows frequent unpredictable hemorrhages many of which require hospitalization. The patient soon learns the hereditary nature of his defect, its seriousness, and the ineffectiveness of the limited facilities for its management. His future is grave. The burden to him and his family is enormous. Medical care is often difficult to provide because he needs help often and badly and there has been so little that could be done for him.

It has been known that the intravenous infusion of whole normal blood or plasma restores the prolonged clotting time toward normal and often stops active bleeding in hemophilia. For the past three years hemophiliac patients have been receiving prophylactically by infusion three to four times weekly substantial amounts of fresh or freshly processed frozen citrated human plasma to prevent the onset of hemorrhagic phenomena, or, if they did develop, to control them more adequately before they got out of hand.

Obviously, aside from the organic manifestations of hemophilia, the emotional and socio-economic ramifications are of great interest. Virtually unexplored, their study would not only provide information essential for adequate management of this disease, but also would delineate a pattern which, in its salient features, might be characteristic of other chronic life-threatening hereditary disorders and, with these points in mind, the following study was undertaken. The beneficial effects of therapy on these aspects of the disease were also followed since only by such study could the total beneficial effect of such therapy be adequately evaluated.—*Benjamin Alexander, M.D.**

INTRODUCTION AND PURPOSE OF THE STUDY

INVESTIGATION of the effect of normal plasma on the coagulation time of hemophilic blood,[1-3] aimed at the prophylactic control of hemophilia, has been under way in the Medical Research Laboratories of the Beth Israel Hospital in Boston since October 1945. The Social Service Department was requested to participate in the study in order to evaluate, in terms of social adjustment, the nature and extent to which patients with hemophilia were handicapped by their illness. The scope of this project was later broadened to ascertain whether and in what way treatment would help the patients overcome obstacles to a normal social life, or whether effective treatment itself might introduce new obstacles requiring solution and adjustment. Therapy consisted of intravenous infusions of freshly processed frozen normal human plasma, generally three to four times weekly.

Hemophilia, an hereditary blood disease of the male, is passed from the female to the male. In cases in which no hereditary factor is evident, the disease is ascribed to a mutation of the genes. The disorder is characterized by delayed blood coagulation and

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frequent and painful hemorrhages into muscles, joints and other parts of the body. The disease is chronic with frequent acute exacerbations during which the patient is confined to bed for periods of time as long as weeks or months. The hemorrhages may be spontaneous or may result from injury or strain; the slightest scratch or minor bruise may cause a severe hemorrhage which may incapacitate the patient for many weeks. Death from uncontrollable bleeding is not uncommon.

Method

The observations reported here are based on the life histories of six patients prior to and during treatment at the hospital. The method of the study was through a series of social interviews by an experienced medical social worker with each patient, and in some instances with members of the family. Initially, the interviews were not directed toward assisting the patients with their problems but rather to gain an understanding of the patients during the course of their illness, both prior to and during the current prophylactic treatment. However, it soon became evident that the scope of the social worker's activity would not be limited to this aspect of the study. Some of the patients' problems pressed acutely for solution so that the patients might be able to make positive use of the medical treatment itself. Certain other patients, in relating their personal histories and feelings and attitudes during the interviews, sought and received assistance from the medical social worker with both their emotional and environmental problems.

The data include the attitudes of the patients and their families toward hemophilia and its sequelae; the meaning of the disease in terms of activity restrictions and handicaps to normal living; the influence of hemophilia on family life, prior to treatment, and the changes following treatment, and the social and financial costs of the illness to the community, and social problems and readjustments created by effective therapy per se.

Case Reports

Case 1. The patient was a 24 year old American Protestant laboratory technician of Ukrainian parentage, the second of three children from a family in the low income group. One of the mother's brothers had died of severe bleeding. A brother of the patient had died at 6 months of age and was thought to have been a bleeder. The patient's diagnosis was established at 18 months of age.

His early life was characterized by frequent hemorrhages necessitating bed care, many hospitalizations, restricted activity, and sporadic school attendance. The patient was treated at home in a nonspecific way from 1921 to 1934. Between June 1934 and July 1941, 10 periods of hospital care totaled 301 days. All costs of medical care were paid from public funds and community agencies provided special diets, glasses, an orthopedic brace and special medications. From the sixth grade through high school, he attended a school for crippled children from which he graduated. He then began the study of bookkeeping, which was abandoned because of an acute exacerbation, and for a short time was a laboratory technician. In August 1942, he was hospitalized in Boston and remained three years, living in a hospital ward in the dual capacity of patient and laboratory technician, at first working for maintenance only, later receiving a small salary in addition.

On October 1, 1945, he took a full time position as a laboratory technician in another hospital concurrent with starting the prophylactic treatment described in this paper. Now he lives in a rooming house on his own resources, for the first time in his life in the community without the protection of home or institution.

During the frequent interviews with the medical social worker, he discussed the difficulties, as well as the satisfactions in his new way of life. He continued to have mood swings, but as time went on his periods of depression were of shorter duration and generally associated with dissatisfaction with work, finances or social activities, rather than with his physical condition. He made friends, had an active social life, joined the Y.M.C.A. and participated in active sports, such as handball and swimming. Gradually, however, he realized that even with these activities he was not entirely happy, and through discussions of his social adjustment, came to the conclusion that his work provided insufficient opportunities for advancement and continued satisfaction. He felt prepared to widen his horizons. Vocational counselling was provided for him. The tests pointed toward greater aptitude for salesmanship or advertising than for technical work. The medical social worker arranged inter-

views for the patient with people in these fields who evaluated his potentialities and gave him expert advice. He was referred to the State Department of Rehabilitation and is now being trained in salesmanship.

While this patient experienced some periods of incapacitation in the 18 months of the study period, none of them kept him from his work for more than a few days. For example, a month after he began treatment he was hit by a thrown ball while playing. Previously, such an accident would have incapacitated him for several weeks, probably requiring hospitalization. On this occasion, however, he had little pain and did not have to interrupt his normal activities. To quote the patient: "I can hardly realize that I am able to continue with my work as any normal person would after having received such an injury, slight to most people, but serious to a hemophiliac."

During the 18 months of medical and social treatment he tested his strengths, matured and gained confidence in his own ability to the extent that he was then ready to start on a new phase of his life. His decision to become a salesman has removed him from the protection of a hospital which he previously felt he required and which his job as laboratory technician afforded for about five years. He knows, however, that he will continue to receive treatment at the hospital and that the medical social worker will be available to assist him when necessary.

Case 2. The patient was a 29 year old American Jewish artist of Russian-American parentage, the youngest of three children, whose mother died when he was 15. One brother died in infancy of hemorrhage. The patient's diagnosis was established at age of 6 yrs. The patient had so many hemorrhagic episodes requiring bed care, either at home or in a hospital, that he received his schooling from home teachers. The family was in the low income group, but always managed to pay minimum hospital charges. Patient's medical care cost the family over $4000.00 between the years 1932-1945. Because of frequent acute exacerbations, it took the patient four years to complete a three year art course. Following this, he worked occasionally, but was always hesitant about taking assignments, fearing he could not finish them because of illness. He was unwilling to accept the limitations imposed by his illness because of his desire to be independent and self-supporting.

This patient was incapacitated by numerous old hemarthroses and hemorrhages into the gastrocnemius muscle, resulting in shortened heel cords and great difficulty in walking. On his first visit to the hospital in November 1945, he was carelessly dressed, in need of a shave and in a state of extreme depression. He was morose, gloomy and unwilling to talk. He looked much older than his 29 years.

Soon after beginning the new therapy, he was able to work regularly without acute exacerbations of illness. Gradually he gained sufficient confidence to search for free-lance work. Skeptical when he began treatment, he gradually recognized the extent of his improvement and was immensely pleased with his increased accomplishment. Security attained through interviews with the medical social worker encouraged and helped him to find remunerative work. His ambition to be independent financially was realized. He was stimulated to do the type of work which he most enjoyed, painting in oils and water colors. Also, he was encouraged to develop his interest in ceramics which may lead to commercialization of his work.

One of his hopes had been an operation to reduce his difficulties in walking due to crippling hemorrhages into his gastrocnemius muscles. This was fulfilled with excellent results within one year after beginning treatment. Although deeply depressed when he began treatment, within the period of study he developed considerable emotional stability. He even learned to accept with equanimity the few and relatively short periods of incapacitation.

Case 3. The patient was an 18 year old American Protestant high school boy. There was no family history of hemophilia. The patient's diagnosis of hemophilia was established at the age of 4 or 5 years. He had 90 hospital admissions prior to beginning treatment at this hospital. The family is in the low income group paying for all care at a minimum rate. For 31 hospital admissions of a total of 354 days, the family paid approximately $2,478.00. Information concerning the cost of the other 59 hospital admissions was not available.

The patient, an only child, grew up in an adult environment. He was quick and active but, because of his disease, was not permitted to play with other children unless his mother was present. She feared he might bruise or otherwise hurt himself. All of his schooling was provided by home teachers through the local board of education until he entered junior high school just prior to beginning treatment at the hospital in April 1946.

Since then he has been able to participate in all group activities at school. Moreover, he has been able to take long hikes, hunt, and drive an automobile. He has an active social life, attending parties

and participating in the functions of a fraternal organization. His interest in girls has become that of a normal boy of his age. He has been absent from school for only a short period during an acute hemorrhagic episode. This, he says, has been the best year of his entire life.

His mother too has found release from great tension. Her discussions with the medical social worker have been directed toward verbalizing her conflicting feelings about her only son's increasing independence and the signs of his "growing up." She has been helped to accept this sudden growth from childhood to maturity.

Case 4. The patient was a 7 year old American Catholic schoolboy of Italian-Polish parentage. He had a 12 year old sister, a 10 year old brother, and twin brothers 9 months old. An infant brother and a maternal uncle have hemophilia. When the patient was 6 months old the diagnosis of hemophilia was suspected, and established when he was 6 years old. The family was in the low income group and could pay only minimum amounts toward the patient's hospitalization which proved to be a burden to them.

Frequent hemorrhages requiring bed care had interrupted the patient's schooling. The mother constantly tried to curb the patient's activity stimulated by his need to imitate his older brother. If the patient injured himself, the father blamed the mother for not giving him proper care, thus intensifying family disunity. Both parents wished to withhold the knowledge of the diagnosis from the paternal family, fearing family disruption.

The patient began treatment at the hospital in June 1946. Social case work services were directed toward making the environmental adjustments necessary to insure the patient's treatments uninterruptedly. His prompt dismissal from school was requested to enable him to come for his treatment immediately after school. From his suburban home, the trip to the hospital required several trolley, bus and subway changes. Occasionally, it was necessary to arrange for automobile transportation to the hospital when he had acute hemorrhagic episodes. The patient's mother required considerable support and assistance in acceptance of the physician's recommendation that overprotection of the child be avoided and that he be permitted to participate, during the period of plasma therapy, in the activities of his older brother and schoolmates.

Case 5. The patient was a 3½ year old American Catholic boy, whose family lived in New Jersey. On learning of the new method of treating hemophilia at this hospital, they brought the patient to Boston. There was no family history of hemophilia. Patient had a normal younger brother, one year old. The patient's diagnosis was established at age of 9 days. Prior to his admission to the hospital, he spent 2½ months in a New Jersey hospital at a cost of $320.00. His parents were indebted for this amount and saw no way of paying it from their low income. Previously, they had paid $528.00 elsewhere for treatment of his hemophilia.

The patient had hemarthrosis of the right knee and walked with a limp. Deprived of the privilege of playing with other children and having always been told to "be careful," the child had grown fearful of most activity.

He began treatment in September 1946. His parents were extremely anxious about the necessary separation from their child, in the hospital 300 miles from his home, too distant for frequent visits. In an interview with them, the medical social worker helped to allay their apprehension through her understanding of, and appreciation for, their problems in raising the child.

By frequent communications with his parents and conversations with the patient, the worker maintained continuity of contact between them and him. The parents were given full details about the patient's everyday life in the hospital. They frequently wrote and telephoned the doctor, whose reports gave them further reassurance. After the patient's discharge from the hospital, the correspondence continued as the mother had need for and requested the interest and assistance of the medical social worker and the doctor.

Case 6. The patient was a 21 year old American Jewish laborer of Russian parentage, the third of five children. An older brother who "bled to death" at the age of 5 years following an accident was probably hemophilic. The diagnosis of hemophilia, suspected when the patient was circumcised, was established at the age of 6 years. His schooling, sporadic because of frequent hemorrhages, was terminated at the eight grade. His work history had been a series of unskilled labor jobs in all of which he had frequent accidents, some requiring hospitalization. His father, an alcoholic, had threatened to put him out of the home; his mother, on the other hand, had always been overprotective of him.

With the beginning of prophylactic therapy in January 1947, the patient was able, with the help of the medical social worker, to give up his former unskilled labor job and to enter high school. The

social worker nurtured his interest in radio and electronics, and, in conjunction with the Massachusetts State Division of Rehabilitation, planned a training program for the patient in a radio school. Lengthening of his right heel cord was under consideration by the physicians, but was postponed. Until this operation is performed, the right shoe will be built up to provide better balance. This shy, withdrawn young man responded so well to the interest of doctors and social worker that he began to develop in a mature way, planning for his future, rather than living haphazardly as in the past. His home, as a result, became much more harmonious. The parents, happy that the patient had improved with treatment, were eagerly in accord with the plans for his rehabilitation.

Discussion

Prior to Treatment

1. Sequelae of Hemophilia and Effect on Attitude of Patients and Families

Four of the six patients were partly disabled because of old hemarthroses and/or shortening of the heel cords. The resultant imbalance in walking had added strain on certain muscles and joints with frequent hemorrhages into these structures. Two patients had always wished to have their heel cords lengthened, but elective surgery had been considered out of the question.

The older patients, "hating the sight of cripples," dreaded their disease, not only because of the acute pain, but also because of the fear of becoming increasingly crippled. The physical deformities became a source of anxiety to them, because of the restrictions and limitations in their activities. Even the 3 year old patient repeatedly said, "The cast will make my knee straight," querying hopefully, "Then, can I run?"

As the patients grew older they feared the assumption of responsibility because they might become ill at any moment and be prevented from fulfilling their commitments. They were afraid to "date" girls, lest an unexpected hemorrhage necessitate cancellation of their appointments. Never knowing when they might become ill, they could not plan ahead, nor travel, nor take vacations away from home, nor even buy theater tickets in advance. One patient remarked that at the age of 6 his horizon was what he could see from his doorstep.

When hospitalized, these patients felt they were frequently regarded as "museum pieces," to quote one patient. Because of the relative rarity of the disease, they were often "on display." As adolescents they found this particularly annoying. They wanted to be normal. Families as well as patients spoke of the insecurity induced in all areas of their lives by the disease. Two of the patients wished they had had infantile paralysis instead of hemophilia. One of them remarked, "If I had infantile paralysis I would know where I stand, what I can do. With hemophilia, I never know when I am going to hemorrhage, so I am always afraid to do anything." Another patient commented with much feeling, "There is a certain glamour to having a heart condition, but no one knows how painful it is to be a hemophiliac." One of the patients from a humble, socially disadvantaged family apparently gained some compensation for his misery through attempts to trace his ancestry to royal families, generally associated in the public mind with hemophilia, or "blood royal."

2. Meaning of Hemophilia in Terms of Activity Restrictions

The activity of these patients was greatly restricted. For the young child it meant restricted play, carefully selected toys with no sharp edges and contact with nothing with which he might injure himself. Immediately, these boys were set apart from other children. They were deprived of sharing in the active sports and rough games of their

brothers and sisters and the neighborhood children. If they attended school, they were restricted from active schoolyard games to prevent falling and injuring themselves. They were not permitted to participate in gymnasium work. Because they were not allowed to go on tramps in the woods or all-day hikes, they could not join the Boy Scouts or the other active neighborhood or school groups. The patient who went to a school for crippled children did not "belong." To quote him, "I was too active to go with the cripples, and I couldn't do what the well boys in the neighborhood did, so I always felt 'in-between.' Even the blind and the deaf boys have strong bodies and can be active."

Because all patients had had many periods of hospitalization, there was no possibility of continuity in schooling. Two of the four older patients had had home instruction for the greater part of their school years. They were, therefore, deprived of the opportunity for group activity, group thinking and stimulation, and friendly attachments with other children.

As the boys grew to manhood there were limitations in the choice of work. Semisedentary occupations requiring no strain were recommended. These are always difficult to find within the sphere of interest and physical capacity of patients. For these patients, there were added complications due to the unpredictability and frequency of hemorrhagic episodes interrupting even otherwise suitable work.

3. Effect of Hemophilia on Family Life

Exhausted by day and night care of the patient with consequent neglect of other members of the family, the parents' absorption in the hemophilic child frequently aroused hostile feelings in other members of the family toward the patient as well as to the parents. The parents of one patient had been advised by reputable physicians to have no more children to avoid the anguish of "seeing their children and grandchildren suffer."

Mothers of two of the patients were in a constant state of fear lest their young sons should hurt themselves. If they did, the husbands always blamed the mothers for apparent neglect of the hemophilic children. All mothers interviewed claimed that they were "nervous wrecks" from the strain. Considerable friction developed in some of the homes, when the fathers or even the patients (as they became informed of the genetics of the disease) blamed the mothers for producing their hemophilic sons, even where there were no family histories of hemophilia. An unusually close companionship apparently developed between most of the fathers and their hemophilic sons.

4. Meaning of Hemophilia to the Community

From the community point of view, both the social and financial costs were great in many directions. Some of the costs are obvious, while others less direct also have significance. There is bound to be a loss due to a continued state of unemployment or irregular school attendance. Providing home teachers is an added financial burden to the community. The cost of hospitalizations and medical care is mainly borne by the community, as only the most affluent are capable of carrying the enormous costs of medical care for recurrent acute episodes year after year.

After Treatment

1. Changes in Patients due to Treatment with Regular Infusions of Plasma

The reactions of the patients and their families to this new treatment is of considerable

interest. From the beginning they were eager for it, because previous treatment had been only palliative while the new type of treatment is preventive as well. After a few weeks they saw marked improvement. Then, the patients began to worry about the possibility that the doctors might not be able to find good veins for regular continuous treatment. In their past experience their veins had been destroyed by surgical transfusions. Later, they expressed apprehension that the veins might not withstand constant treatment, and that treatment might have to be discontinued if too much scarring occurred in the veins. As time went on, and they observed that their fears did not materialize, they expressed concern that their treatment might be discontinued when the research studies were terminated. Reassured on this point, their next doubts involved the "human element"—fear that there might not always be enough human plasma available.*

One by one, these fears and doubts vanished as treatment proceeded. The one practical problem before them became the adjustment of work and school hours to hospital attendance for treatment. Two patients travelled 80 miles to and from Boston for each treatment and have continued to do so regularly for many months. The benefits of the treatment proved to them beyond a doubt that all adjustments have been, in the long run, worth making. Those who previously were "handicapped invalids" were now able to consider themselves, in the words of one of them, "normal individuals with a handicap."

With regular treatment of infusions of plasma, these six patients have had few hospitalizations or periods of incapacitation. This concrete evidence of their improved conditions has greatly encouraged the patients and reduced their depressive states. Furthermore, every hemorrhage does not now necessarily mean going to bed, for minor hemorrhages no longer incapacitate them. They have gained security in their ability to be active.

During an interview with one of the patients one day, he suddenly said—"At this moment I'm hemorrhaging in my mouth and I just had a hemorrhage in my arm. Before, this would put me to bed for a month. Now, it doesn't even interfere with my work."

Two of the mothers informed the medical social worker that previously when their sons had hemorrhages they were up with them night after night because of the excruciating pain. Now, they were pleasantly surprised to find that the boys suffer less, and they can all get some sleep.

As a result, family life has become more normal for the patients and other members of their families as well. Their mothers have a "new lease on life." They have renewed old acquaintances and made new ones. No longer are they tied down by constant dread of illness of the hemophilic member of the family. Strained parental relationships have practically vanished. The need to blame the mothers for not giving the hemophilic sons the proper care and attention has passed. One mother stated that for the first time since the onset of the son's illness, she is "now able to live." She feels relaxed, has gained weight and recently learned to drive a car, which previously she had been too nervous to do.

One important result from a medical point of view is that one patient has been able to undergo an elective operation, lengthening of the heel cords. The fear of surgery always had loomed up as one of the greatest anxieties of both patients and parents alike. The possibility of being able to have an elective operation has further stimulated their self confidence. If they can undergo corrective surgery for the crippling from

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* The plasma used was provided from the Beth Israel Hospital Blood Bank with the cooperation of the Volunteer Blood Donors of the Beth Israel Hospital Ladies Auxiliary.

hemathrosis and shortened heel cords, this is further concrete evidence that their hemophilia is under relative control and some correction of the crippling can take place.

Important as it is for these boys and young men to work, whether gainfully or at school, even more important is the possibility of their attaining personal and social development. All six patients were enabled to make friends more readily than before. One engaged in his favorite sport of hunting. Another's interests were directed toward handball and other gymnastic exercises. His physical and psychologic gains brought about the realization of an ambition to become a member of the local Y.M.C.A. A third patient gained enough security in his physical condition to take short trips for the first time. Previously the only recreational outlet for two patients had been excessive reading. They had lived vicariously through the characters in their books in an unrealistic world of day-dreams. The four older boys have, since treatment, taken a more active interest in social activities. All four learned they could plan in advance, believing they could keep their appointments. One young man has even begun to plan marriage soon.

The effects of the new treatment of hemophilia on their social development has differed with the personalities, ages, social activities and interests of these six patients.

2. Effect of Hemophilia and Its Treatment by Regular Infusions of Plasma on the Personalities of the Patients

The improvement in the general physical conditions of these patients has had a stabilizing effect upon them. Their personality patterns have, to a certain extent, been altered with their increased security. Emotional maturity and growth have been demonstrated by greater independence and increased ability to make the adjustments necessary for transition to a normal way of life.

In an article published some years ago on the social adjustment of a group of chronic cardiac patients treated by total thyroidectomy,[4] it was noted that the personality changes in the patients following improvement in their physical conditions "depended on the constructive elements inherent in their individual personalities." Although the cardiac patients were older and their potentialities for emotional growth and adjustment were, perhaps, somewhat limited, the same observation seems to hold for the older patients in the groups of hemophiliacs. Each individually benefited from his improved physical status only in proportion to the degree of his emotional maturity.

All of the patients studied had been overprotected. This had made some more desirous of remaining dependent, while others demonstrated a strong drive for independence. One had expressed a need for independence, but his behaviour suggested a continuing strong need for dependence. Perhaps his own statement is significant: "The doctor took away my hemophilia, now I have nothing to lean on." Apparently, previously he had always attributed his inadequacies to his disease. Now he fixes responsibility for his depressed feelings on environmental factors, rather than on his physical condition. Another patient has shown more stability and more security although he is still depressed at times. He has shown a steady and increasing interest in his work and has applied himself to it seriously even under adverse conditions. Both patients have taken much more interest in their general physical appearance. All of the patients have had psychiatric evaluations, and psychiatric assistance has been available to them. The two older patients have made use of this service as they have felt the need and it is hoped this will continue to be the case.

It is exceedingly difficult to evaluate properly a new prophylactic therapeutic approach in hemophilia in view of the well known remissions and exacerbations of this disease.[2] Moreover, any organized sustained interest by doctors and medical social case workers in patients discouraged by the hopelessness of the medical management of the disorder would result in a more buoyant outlook, general optimism and a feeling of well being. Accordingly it is recognized that the subjective feeling and attitude of the patients cannot be considered indisputable evidence of the efficacy of the treatment. Final evaluation of this particular approach in the prophylactic management of hemophilia must await further study.

Summary

A study has been made of six patients treated for hemophilia by repeated frequent infusions of plasma.

Prior to beginning treatment these patients were semi-invalids, hospitalized frequently for periods of weeks and months and handicapped in their adjustment to normal social life. Since treatment they and their families have gained a feeling of confidence, without fear of hemorrhage "hanging over their heads." They know that if a hemorrhage occurs, it probably will not incapacitate them, but that even if it does, the period of incapacitation will be comparatively short. Our observations indicate great improvement in the lives of the patients studied. Whatever the future may hold for these patients, they have acquired a new outlook on life and many positive experiences. Also, from this study some insight has been gained into the social component of this disease and of the problems both solved and created by effective treatment.

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Spanish Abstract

Adaptación Social de Seis Pacientes con Hemofilia: Antes y Durante el Tratamineto Profiláctico

Se ha hecho un estudio de seis pacientes que se trataron por hemofilia mediante infusiones de plasma frecuentes y repetidas.

Antes de principiar el tratamiento estos pacientes estaban semi-inválidos, hospitalizados frecuentemente por períodos de semanas y meses e impedidos en su adaptación a la vida social normal. Desde el tratamiento ellos y sus familias han cobrado confianza, sin tener sobre ellos aquel temor de hemorragia. Ellos saben que si hay hemorragia que probablemente no los incapacitará; pero si quedan incapacitados que el período de incapacidad será relativamente corto. Nuestras observaciones indican gran mejoría en las vidas de los pacientes estudiados. Han adquirido un modo diferente de ver la vida y muchas experiencias positivas. También se had logrado de este estudio un discernimiento en el componente social de esta enfermedad y de los problemas que han sido resueltos y creados mediante tratamiento efectivo.

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ANOMALOUS CHANNEL BETWEEN AORTA AND RIGHT VENTRICLE

Report of a Case

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A 13-MONTH-OLD boy, whose cardiac studies over a seven month period had suggested the presence of a large ductus arteriosus, died of a purulent tracheobronchitis. Autopsy revealed an insignificant patent ductus and a unique vascular tract, which arose beside a normal coronary artery in the left posterior sinus of Valsalva, and passed into a small side chamber of the right ventricle, along the lower border of the pulmonary conus. This case exemplifies a group of cardiovascular anomalies which resemble a patent ductus arteriosus clinically and may be operated on as such.

CASE HISTORY

The patient, a Negro boy 13 mos. old, was admitted to the hospital with the tentative diagnosis of nasopharyngeal diphtheria. Symptoms of fever, nasal discharge and increasing respiratory difficulty had begun 4 days previously and had not responded to chemotherapy.

Examination revealed a well developed and nourished, acutely ill infant in moderate respiratory distress, but without retraction or laryngeal stridor. He was pale but not cyanotic or restless. The temperature was 40.0° C., the pulse 130/min. and the respirations 30/min. The blood pressure was 98/65 mm. Hg. A profuse nasal discharge was present. The alae nasi were excoriated. The throat was markedly injected and the lower edge of a grey membrane was visible in the nasopharynx. No retropharyngeal mass was felt. Auscultation of the lungs was unsatisfactory but there was normal resonance. The heart appeared enlarged with the apex beat in the left anterior axillary line. There was a strong precordial thrust and a pronounced thrill was felt along the left sternal border throughout the cardiac cycle. A loud, machinery-like murmur filled systole and diastole and was transmitted to the left axilla and to the back. It was loudest in the third and fourth left interspaces next to the sternum. Both thrill and murmur seemed close to the surface. The liver was felt 1 cm. and the spleen edge 2 cm. below their respective costal margins. There was no clubbing or edema. Blood and urine studies were noncontributory. Throat smears and cultures were negative for C. diphtheriae.

The diagnosis of acute nasopharyngitis and laryngotracheitis was made. It was felt that the cardiac lesion was a patent ductus arteriosus. Diphtheria antitoxin 40,000 u. was given in the admitting room. On a program of penicillin, sulfadiazine and supportive parenteral fluids there was some improvement in temperature and appearance but the abundant nasopharyngeal secretions made frequent aspiration necessary. On the second night the patient expired suddenly and unexpectedly at 5 a.m.

PAST HISTORY

The patient was born at Herman Kiefer Hospital, and passed an uneventful neonatal period during which no mention was made of positive cardiac symptoms. At 6 mos. of age the patient was hospitalized locally for bronchopneumonia. A generalized machinery-like cardiac murmur was described at this time. At 7 mos. he was seen in the Outpatient Department at the Children's Hospital of Michigan, where a to-and-fro cardiac murmur was described, heard best in the 3rd and 4th left parasternal interspaces. A month later, he was admitted to the same hospital with bronchopneumonia

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which responded promptly to chemotherapy. Growth was normal and there had been no prior episodes of dyspnea or dysphagia. Cardiac roentgenograms (Fig. 1) at this time were reported as showing "the heart to be enlarged to both right and left, with accentuation of the pulmonary conus and some posterior displacement of the esophagus. The cardiac measurements were IDC 15.5 cm.,

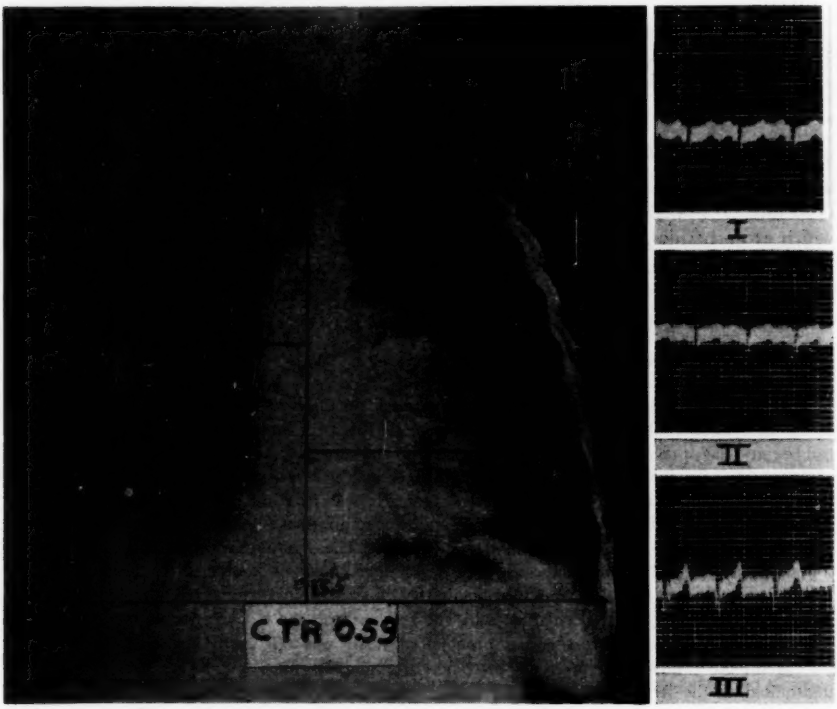

FIG. 1. A-P view of chest for heart size. Enlarged to both right and left with accentuation of pulmonary conus.
FIG. 2. ECG. Normal tracing with sinus tachycardia.

ML 6.5, MR 2.5, GV 4.0, CTR 0.59." The ECG (Fig. 2) was within normal limits. The diagnosis of a patent ductus arteriosus was entertained, and operative correction was to be considered when the patient became older.[1]

AUTOPSY FINDINGS

Of greatest interest was the heart, the apex of which was at the level of the left 6th rib just lateral to the mid-clavicular line. Pericardium was normal. Anteriorly the ventricles had a globular outline with a deep apical groove. Right auricle was dilated and the venae cavae were normally formed. Foramen ovale was incompletely closed with a functional opening about 1 mm. in diameter. Tricuspid ring was normal. Right ventricle was hypertrophied and moderately dilated. Pulmonary conus was enlarged and presented two outlets. The first of these led to a normally formed, competent pulmonary valve and artery. The second (Fig. 3) was located immediately beneath the first and was separated from it by a ridge of myocardium. It narrowed in funnel fashion to form an endothelialized tract extending from the chamber of the right ventricle to the aorta. This tract measured 5 mm. at its narrowest diameter and passed beneath the pulmonary artery to the right of the left coronary artery and entered the aorta in the sinus of Valsalva behind the left posterior aortic cusp.

This sinus measured 10 mm. in depth whereas the other two were only 7 mm. deep. Just anterior and to the left of the opening of this channel was the opening of the left coronary artery which followed its usual course and distribution. Right coronary artery was in its usual position and had its usual course. Just anterior to its mouth was a dimple which was not patent to probing. Mitral and aortic valves were normal. There was a tiny ductus arteriosus, patent only to a hairpin and measuring 1 cm. in length.

FIG. 3. Drawing of heart with cavity of right ventricle exposed; arrow points to anomalous vascular tract. The opening in aorta distal to valve cusps may be seen.

Both lungs were slightly edematous and appeared to be well aerated. The trachea and bronchi were injected and contained abundant mucopurulent material, from which Staph. aureus and Str. hemolyticus were cultured. The peritracheal and peribronchial lymph nodes were markedly enlarged. The liver was slightly larger than normal and the spleen was twice normal size. There were a number of agonal intussusceptions all easily freed and with only slight vascular change.

Microscopic sections of the heart showed nothing which might have explained the sudden death on a cardiac basis.

DISCUSSION

Direct communications between aorta and pulmonary artery above the level of the sinus of Valsalva have been reported and are presumably the result of a developmental defect in the partitioning of the truncus arteriosus. Hektoen[2] reviewed nine cases and added one of his own having a 1.5 cm. defect just above the aortic cusps in a newborn. Potts[3] recently operated on a child who was found to have a communication of this type between the aorta and the pulmonary artery close to the heart. Abbott[4] has suggested that these abnormal channels have a phylogenetic homologue in the heart of certain reptiles, notably the crocodile, in which the foramen of Panizzae connects the right pulmonary artery and the right aorta at this level. Catheterization of the pulmonary artery in these cases would demonstrate a shunt of arterial blood into the pulmonary artery a short distance beyond the semilunar cusps, closer to the heart than found in a patent ductus arteriosus.

A second type of abnormal communication in this region is an aneurysm of a sinus of Valsalva.[1, 5] These are usually of the right sinus and may rupture into the right auricle or right ventricle. Clinical manifestations are absent until rupture occurs. An instance of aneurysmal dilatation of all three sinuses has been reported.[6]

A third type, to which the case here reported seems more closely related, is illustrated by Livingston's case[7] of a three month old infant who had a passage from the aorta into the right heart, opening above and below the tricuspid valves. Jacobi and Heinrich[8] reported an 18 month old infant with a fistulous tract, evidently congenital, which led from an aortic opening between the coronary orifices and passed into the right ventricle just below the posterior commissure of the pulmonary cusps. Abbott[9] refers to others and feels that such communications may be explained by the torsion theories of cardiac chamber development, as summarized by Spitzer.[10]

A more recent and more critical account of the partitioning of the embryonic truncus arteriosus to form the aorta and pulmonary artery has been given by Kramer.[11] This interpretation is followed by Patten.[12] According to these two sources the partitioning of the truncus begins with the formation of a pair of ridges of endocardial cushion tissue, the so-called truncus ridges, which bulge progressively farther into the truncus lumen and ultimately meet and fuse with each other to divide it. The partitioning of the truncus begins at its aortic arch end and progresses spirally toward the ventricle. Defects connecting the aortic with the pulmonary trunk above the level of the semilunar valves, as in the cases reported by Hektoen,[2] are attributable to defects in this part of the septal complex.

At the point of transition from truncus to ventricular conus, three localized pads of endocardial tissue form in the aortic channel and a similar group of three develop in the pulmonary channel. These are the primordia of the semilunar valves. Below the level of the valves the longitudinal ridges which first appeared in the truncus are continued, under the name of conus ridges. The conus ridges grow toward the crest of the interventricular septum and take part in the ultimate closure of the interventricular foramen by the formation of the pars membranacea of the interventricular septum.

Of particular interest in connection with the present case is the way the coronary arteries develop as new vessels during the seventh week. They push out as small vascular sprouts just distal to the primordial pads that are the forerunners of the aortic semilunar valves. Thence they extend into the developing myocardium, communicating both with the developing coronary veins and to a certain extent, also,[13] with the intertrabecular spaces of the ventricular myocardium. As development progresses these intertrabecular spaces are greatly reduced in size, and since they have been endothelially lined from the outset they merge without demarcation into the rest of the vascular bed of the myocardium. On this basis Patten regards the venae minimae cordis as representing reduced remains of the intertrabecular spaces of the embryonic heart.

In the light of this developmental background, it seems logical to interpret the abnormal communication in this case as an accessory coronary artery which had retained, and secondarily enlarged, part of the old system of intertrabecular spaces in the ventricular myocardium. Patten and Barry of the Anatomy Department of the University of Michigan, after examination of this heart, suggested such a possibility as the best explanation for the anatomic features seen. If this interpretation is accepted, it is illogical to apply the term aneurysm, with its implication of an underlying pathologic process, to

what is really the retention and relative enlargement of an old embryonic channel.

In this case there was an intact endothelial lining throughout the tract, with no remnant of a ruptured aneurysmal sac and no evidence of aortitis. Although the tract was about three times the diameter of the normal sized left coronary artery beside it, the presence of double coronary openings in the right posterior sinus suggests that the anomalous passage may have been a large accessory coronary artery, which had anastomosed early in development with intertrabecular spaces in the myocardium and thus established communication with the chamber of the right ventricle.

In retrospect the anomaly in this patient could have been diagnosed as an intracardiac communication between the aorta and right ventricle by 1. the machinery-like murmur and thrill, lower and more superficial in the thorax than those of a patent ductus arteriosus; 2. the discovery on cardiac catheterization of an abnormally high oxygen saturation of right ventricular blood; 3. presumptive exclusion of an interventricular septal defect by the diastolic element in the murmur, and 4. failure of the catheter to enter the left ventricle directly.

Summary

The occurrence of a congenital vascular tract between the left posterior aortic sinus of Valsalva and the right ventricle in a 13 month old boy is reported. A group of cardiovascular anomalies which clinically resemble a patent ductus arteriosus is discussed, and the help which cardiac catheterization may give in confirming the diagnosis is indicated.

Acknowledgment

We are indebted to Dr. W. L. Brosius for the autopsy findings.

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SPANISH ABSTRACT

Canal Anómalo entre la Aorta y el Ventrículo Derecho

Se presenta el caso de un varoncito de trece meses de edad, cuyos estudios cardíacos por un período mayor de siete meses surgirieron la presencia de un canal arterioso grande, y guien murió de una tráqueobronquitis purulenta. La autopsia reveló un canal patente insignificante y una arteria vascular única en el seno posterior de Valsalva, que pasó a un lado pequeño de la cámara del ventrículo derecho, a lo largo del borde del cono pulmonar. Este caso ejemplifica un grupo de anomalías cardiovasculares que se parecen clinicamente a un canal arterioso patente, y se pueden operar como tal.

Se dan examines de literatura y teorías con respecto al desarrollo embriológico. Se indican los criterios diagnósticos y la ayuda que puede dar el cateterismo cardíaco al confirmar la diagnosis.

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APICAL DIASTOLIC HEART SOUNDS IN ACTIVE RHEUMATIC FEVER

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IN FOLLOWING young patients with active rheumatic fever, two diastolic auscultatory findings at the cardiac apex commonly present themselves for evaluation. These are the diastolic third heart sound and the early apical diastolic murmur of active rheumatic carditis. Both of these apical diastolic sounds result from events which occur in the period of rapid diastolic filling of the ventricles. The close association of these two auscultatory phenomena in the cardiac cycle and in actual clinical observation suggested an analysis of their interrelation, which is the subject of this study.

I. CLASSIFICATION OF ADVENTITIOUS HEART SOUNDS HEARD IN DIASTOLE

A host of titles have been applied to extra sounds heard in diastole. In a recent review, Evans[1] stressed the confusion resulting from the varied nomenclature and listed some 20 different names given to sounds heard in this period of the cardiac cycle. Most classifications are based on the position in time which this sound occupies in relation to the first and second heart sounds. Gallop rhythm is the usual term applied to the sequence of three sounds, and probably the most useful nomenclature for these sounds has been offered by Wolferth and Margolies,[2] who suggested the terms protodiastolic and presystolic gallop sounds, depending on their relative time location in the diastolic interval. They described a third or summation type of gallop sound which represents the fusion of the two above mentioned types in the presence of tachycardia and a shortened diastolic period.

The third sound of protodiastolic gallop rhythm cannot be differentiated from the physiologic third heart sound by its acoustic quality. The former is the term arbitrarily applied to a third heart sound when it is heard in the presence of circulatory disturbance or disease. In dealing with children, this differentiation depends upon knowledge of the presence or absence of this sound prior to the onset of the disease.

II. DIFFERENTIATION OF THE THIRD HEART SOUND AND REDUPLICATED SECOND HEART SOUND

The early English clinicians, Still[3] and Cheadle,[4] in tracing the development and progression of apical murmurs in rheumatic fever, referred to the third heart sound as a reduplication of the second sound. More recent observations have, however, demon-

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asynchronous closure of the mitral valves on one hand and the physiologic second and third heart sounds on the other. The interval between the components of a split second sound has thus been shown to be of the order of 0.05 to 0.06 sec., while the period measured between the onset of the second heart sound and the third heart sound is usually three times this interval, or approximately 0.13 to 0.18 sec.[2] Such a difference is usually detectable by the trained observer. Again, the two components of a reduplicated sound are identical in quality and pitch, while the third heart sound is distinguishable from a second heart sound by its lower pitch and dull, thud-like character. Finally, reduplicated second heart sounds are most frequently heard at the base of the heart and along the left sternal border, while third heart sounds are most apparent at the apex or slightly above and to the right of this point.

III. The Concept of Apical Diastolic Murmurs Without Structural Valvular Change

Apical diastolic murmurs in rheumatic heart disease have traditionally been considered an indication of organic valvular change. More recently, however, there has been evolved the concept of a diastolic murmur without structural deformity of the valve. While it is certainly true that diastolic murmurs almost always indicate some serious form of cardiac derangement, the literature quoted below indicates that structural valvular deformity can no longer be invariably presumed when cardiac auscultation reveals a diastolic murmur.

The first exception to the original proposition of Laennec and his contemporaries that the apical diastolic murmur was pathognomonic of stenotic changes in the mitral valve was offered by Austin Flint, who demonstrated the possibility of an apical presystolic murmur in the presence of aortic regurgitation and normal mitral valve leaflets. In rapid succession, several other situations were described in which no abnormality of the mitral valve was found at necropsy to explain the presence of an apical diastolic murmur during life. Fisher[5] in 1894 and Phear[6] during the following year presented series of patients who had neither stenotic changes of the mitral valve nor aortic regurgitation, but who showed diastolic or presystolic apical murmurs. Many of these patients were found to have adhesive pericarditis or left ventricular hypertrophy or dilatation, resulting from other pathologic processes. Gossage,[7] in 1909, minimized the role of valvular deformity in the production of the early murmurs of rheumatic carditis, and stressed the part played by myocarditis and the effect of toxins on heart muscle. This investigator also disregarded the minute vegetations found on the valvular margins at necropsy as a causative factor for the murmur. Sheldon[8] considered the commonest diastolic murmur of childhood to be the one encountered during the early phases of active rheumatic carditis and pointed out its evanescent character. In the American literature, this phenomenon was confirmed in the rheumatic patient by the classical reports of Wood and White[9] in 1923 and Bland, White and Jones[10] in 1935. These authors presented lengthy series with studies at autopsy which demonstrated conclusively that apical diastolic murmurs may occur in rheumatic carditis in the absence of gross valvular deformity.

In the course of a systematic clinical investigation of patients with active rheumatic fever, the interrelation between the apical diastolic third sound and the early diastolic murmur became so noticeable that a quantitative study of this relationship was under-

taken. Such a possible relation between the occurrence of these two adventitious sounds has been suggested in the past. Still[3] noted the frequent finding of a third heart sound which gradually became prolonged and tailed off into a decrescendo diastolic murmur extending into mid-diastole. He also emphasized the transient nature of this murmur. More recently this possible sequence of events has been demonstrated by phonocardiographic methods by McKee[11] and by Taquini, Massel and Walsh.[12]

Conventionally, the term mid-diastolic murmur has been applied to the short, blowing, decrescendo murmur which follows the third heart sound in active rheumatic carditis. The use of this nomenclature is subject to some criticism since the onset of this murmur bears a constant time relationship to the third heart sound, and occurs well within the first third of diastole in the slowly acting heart. Therefore, the murmur begins within the first third of diastole and might better be termed the early diastolic murmur of active rheumatic fever rather than the mid-diastolic murmur. When this sound becomes more prolonged, as it usually does, it may extend into the mid-portion of diastole and beyond. These relationships are clearly evident in the heart beating at a normal rate but become more obscure in the presence of a tachycardia. The term early diastolic murmur will, therefore, be employed in this discussion.

Material and Methods

Included in this study is a group of 400 patients admitted to the wards and clinics of The Children's Hospital of Philadelphia, The Hospital of the University of Pennsylvania, The Philadelphia General Hospital, Philadelphia, Pa., and The Children's Seashore House for Invalid Children in Atlantic City, N.J., between the years 1943 and 1948, in whom the diagnosis of active rheumatic fever was made at some time while they were under observation. Consecutive cases were accepted providing they fell within the age limits of 3 and 20 years and demonstrated unequivocal evidence of rheumatic activity. No unusual predominance of either sex was observed. Approximately 50% of the patients studied were Negroes.

Each patient was examined on at least one occasion each week during his convalescent period, and two, three or more times per week during the acute stages of the disease, depending upon the rate of change of cardiac findings. Detailed records were kept of these changes. All of the observations were made or confirmed by at least one of the authors.

The data were collected in two main sub-groups. The first group consisted of acutely ill patients followed on the wards of The Children's Hospital of Philadelphia, The Hospital of the University of Pennsylvania and The Philadelphia General Hospital. These patients were admitted shortly after the onset of their acute illness and presented the protean manifestations of active rheumatic fever. The second group consisted of those followed in the Rheumatic Fever Clinic of The Philadelphia General Hospital and on the wards of The Children's Seashore House for Invalid Children. These patients were convalescing from their acute illness. Many of the individual patients were studied from the extremely active phase of their disease to complete quiescence while in the hospital wards and convalescent home and later in the outpatient clinic, so that a complete cycle or series of cycles of the disease could be traced in chronologic order. In all of the patients admitted to this study, the rheumatic process was definitely active. Patients with active chorea as the only manifestation of rheumatic infection were not included. All patients were followed with weekly determinations of the erythrocyte sedimentation rate and other laboratory determinations necessary for the evaluation of rheumatic activity.

Results

Of the 400 patients with active rheumatic fever, 115, or 29% had on at least one occasion while under observation either a third heart sound or an early diastolic apical murmur. In some of these patients only one of these two auscultatory findings was present, and it remained unchanged throughout the period of observation. In others,

these diastolic sounds were found to occur in definite sequence. In several cases the third heart sound gradually became prolonged into a diastolic murmur, subsequently reduced in some cases to a distinct third heart sound as the rheumatic process subsided. In other patients, among those who were not brought under observation until a diastolic apical murmur was well established, this murmur was found to regress and be replaced by a third heart sound. Two patients who had passed through this sequence developed a murmur again during a subsequent reactivation of the disease process. Table I indicates the number of patients in each of these categories as well as their distribution in the acute and convalescent groups.

TABLE I

SEQUENCE OF ADVENTITIOUS DIASTOLIC SOUNDS IN PATIENTS WITH RHEUMATIC CARDITIS IN ACUTE AND CONVALESCENT GROUPS

	Acute Group		Convalescent Group		Total No.
	No.	Per Cent	No.	Per Cent	
Third heart sound alone	23	85	4	15	27
Early diastolic murmur alone	29	86	5	14	34
Third heart sound followed by early diastolic murmur	17	85	3	15	20
Early diastolic murmur followed by third heart sound	7	30	16	70	23
Third heart sound followed by early diastolic murmur reverting to third heart sound	5	55	4	45	9
Early diastolic murmur followed by third heart sound reverting to early diastolic murmur	1	50	1	50	2
Total No.					115

In each of the patients in whom an early diastolic murmur was heard at any time, there was also invariably present at the apex a blowing systolic murmur, usually high pitched in nature and transmitted a variable distance to the left, indicating some degree of regurgitation at the mitral valve. None of the patients with a diastolic murmur included in this study developed this murmur during a severe episode of cardiac failure or an agonal state. Thus no great departure from the normal cardiac physiology need be considered in these patients at the time.

From Table I it is evident that the third heart sound and early diastolic murmur commonly occur in sequence. A total of 54 patients, or approximately half of those who showed either sound, demonstrated this sequence in one form or another during the period of observation. Variations in this sequence are well correlated with other evidence of progression or regression of the rheumatic process. This is especially well brought out by the fact that the change from third heart sound to murmur occurred

in 85% of the instances in the acute group, as compared with 30% among patients in the convalescent phase, while the corresponding percentages for the reverse transition from murmur back to third heart sound were, respectively, 15 and 70. These data also emphasize the transient nature of this early diastolic murmur and further suggest that its origin does not lie in any permanent, irreversible, structural valvular change.

It was often not simple to determine clinically at precisely what point a clear cut third heart sound changed to a diastolic murmur. There was frequently an intermediate stage in which an indistinct quality replaced the usually abrupt ending of the third heart sound. The duration of the third heart sound then appeared longer than that expected of a heart sound alone. This apparent prolongation or tailing off of the third heart sound usually took the form of a soft, short, decrescendo, blowing, low-pitched sound which became progressively longer, and perhaps much later assumed a somewhat rumbling quality. The transition from third heart sound to a definite murmur could be discovered in any stage of its progression in either direction from a barely detectable roughening of the third heart sound to a definite blowing or rumbling mid-diastolic murmur of easily appreciable length. It must be stressed that in the presence of severe tachycardia it is frequently impossible to determine by auscultation alone in exactly what portion of diastole an extra sound is occurring.

Discussion

I. Other Clinical Evidences for an Interrelation Between the Third Heart Sound and Apical Diastolic Murmur in Active Rheumatic Carditis.

In addition to the interrelated findings of apical diastolic third sounds and murmurs presented above, there are several clinical observations which suggest some relationship or common ground in the mechanism of production of these adventitious sounds. Both of these sounds are best heard at the apex or slightly to the right and cephalad of the apex. It is also not uncommon to hear both sounds in the same patient simultaneously. In a localized area near the apex an early diastolic murmur may be audible, while in a larger concentric circle surrounding this first area a third sound with its characteristic abrupt termination is evident. Certain physical maneuvers which are at times helpful in bringing out more clearly the third heart sound, such as placing the patient in the left lateral decubitus position, exercising the patient and elevating the lower limbs, also accentuate this diastolic murmur in many instances, or in some cases may cause an early diastolic murmur to replace or be added to a third heart sound. The transient nature of the third heart sound is also shared by the early diastolic murmur of active rheumatic carditis.

More evidence for the association of these two diastolic sounds is offered by phonocardiography. By this technic it is frequently possible to demonstrate at a single location on the precordium the presence of a distinct third heart sound, followed immediately by a diastolic murmur. The differentiation of these two portions of the combined diastolic sound is, however, not readily made by ausculation alone. For this reason any series of vibrations of greater duration than that of a heart sound alone was considered in this study to be a murmur, and a further breakdown was not attempted on clinical grounds.

II. Theories of Causation of the Third Heart Sound and Early Diastolic Murmur Suggesting a Common Background in the Mechanism of Their Production.

A brief review of some of the events which occur in the cardiac cycle during diastole will be helpful at this point. The portion of diastole following the opening of the

auriculo-ventricular valves is the period during which the ventricles are filled with blood from the auricles. This period has arbitrarily been divided into three phases. The first is the stage of rapid inflow which follows immediately after the opening of the tricuspid and mitral valves. During this period the pressure in the auricles is high while that in the ventricles is relatively low. This pressure gradient results in the rapid passage of blood from auricles to ventricles and thus accounts for the major portion of ventricular filling. A period of diastasis follows, during which the pressure in the two chambers is more or less equal and flow is minimal, the flow being maintained by return of blood to the auricles through the great veins. It is at the expense of this period that diastole is shortened when the heart rate becomes rapid. The final period of diastolic filling occurs with contraction of the auricles and ends with the closure of the auriculo-ventricular valves which ushers in ventricular systole.

Normal jugular pulse tracings were found by Gibson[13] and Hirschfelder[14] to show a distinct wave in early diastole, coinciding in time with the third heart sound and corresponding with the period of rapid inflow. In conformity with this finding, it is generally agreed that the rapid passage of blood from auricles to ventricles during early diastole produces the vibrations audible as the third heart sound. Much disagreement, however, centers about the exact tissue which vibrates to produce this sound. There are three distinct points of view on this question. Lewis and Dock[15] suggest that the valves are the origin of these vibrations. In terms of their theory, the valvular leaflets are thought to be refloated and partially closed by pressure on their under surfaces during early diastole by the filling of the ventricles. This is taken to interfere with later inflow of blood and so to result in vibrations of the leaflets. Smith[16] and Boyer[17] believe in the muscular origin of the third heart sound. The former author demonstrated, in experimental animals, that the third heart sound persists when the venous inflow to the heart is cut off and the cuspid valves immobilized by splints. He attributed the sound to the sudden distention of the ventricular wall during the filling process. Boyer was able to record third heart sounds from the exposed hearts of dogs, thus ruling out the chest wall as a third possible source of the vibrations in question, as had been suggested at one time by Wiggers, et al.[18]

Underlying these controversial explanations, there are certain points of agreement. The youthful heart with its relatively soft, pliable musculature favors the production of a third heart sound. Rapid return of venous blood to the heart with increased intra-auricular pressure makes for the more forceful flow of blood through the auriculo-ventricular valves during early diastole and thereby has a similar effect. It is for this reason that the third heart sound can frequently be clinically demonstrated in the normal child by such maneuvers as exercising the patient, elevating the lower limbs and applying pressure to the abdomen. Similarly, in the acutely inflamed heart of active rheumatic fever, both factors, the easily distendable myocardial structure and the increased blood flow through relatively normal auriculo-ventricular orifices, continue to favor the production of the third heart sound.

The mechanism of production of the early diastolic murmur of active rheumatic carditis has also been given several explanations in the literature. The most commonly accepted explanation holds that a relative stenosis of the mitral valve exists because of dilatation of the left ventricle in the presence of a normal-sized mitral ring. Dilatation of the left ventricle is undoubtedly common during active rheumatic involvement of the heart, especially in the presence of the mitral insufficiency which almost invariably

precedes the development of the early diastolic apical murmur. The flow of a liquid in a rigid vessel through a relative constriction produces turbulence if the flow is sufficiently rapid. This depends upon the rapidity of flow being uneven and greatest at the constriction. Thus a dilated ventricle is adequate to explain turbulence without any abnormal constriction at the mitral valve.

Bramwell[10] has pointed out that there are two factors in the production of an obstructive murmur: the size of the orifice and the velocity of blood flow. There is an inverse mathematical relationship between the degree of stenosis and the velocity of blood flow necessary to produce an obstructive murmur. If stenosis is mild, the increased blood flow resulting from exercise will therefore bring out a murmur. There is no auditory line of demarcation between anatomic stenosis due to a narrowed orifice and physiologic stenosis due to an increased rate of blood flow. Thus, increased blood flow *per se* may theoretically produce an obstructive murmur at a normal valve. The pathologic changes present in active rheumatic carditis may cause an increase in the velocity of flow of blood through the heart in several ways. In the presence of tachycardia there is an increase in the velocity of blood flow. This acceleration is most marked during diastole since this part of the cardiac cycle is shortened to a greater extent than is systole for any given increase in cardiac rate. The anemia classically associated with rheumatic fever causes an increase in the volume of blood flowing through the heart and thereby contributes to more rapid velocity of blood flow. The decreased blood viscosity accompanying anemia also favors the production of a murmur, since decreased viscosity enhances turbulence in the current of blood. Also the presence of an inflammatory, febrile disease *per se* increases the flow of blood through the heart. Finally, Taquini, Massell and Walsh[12] suggested that the amount of blood appearing in the left auricle is increased in the presence of mitral regurgitation. By further increasing the volume of blood which must pass through the mitral valve, conditions are again improved for the production of a murmur.

Precisely which tissue vibrates to produce the sound interpreted as a murmur is once again difficult to determine. Eddies produced in the rapidly moving blood stream may cause vibrations of the valve leaflets which are usually somewhat rigid at this stage because of the changes due to mitral insufficiency; or further distention of a diseased atonic myocardium may be the source of the sound. The relatively thin chest wall and ventricular wall in children also favors sound transmission and detection.

It would appear, then, that the same factors which are thought to be responsible for and enhance the production of the third heart sound also favor the occurrence of the early diastolic murmur of active rheumatic carditis. Factors which tend to increase the rate of flow of blood through the auriculo-ventricular orifices during the period of rapid filling contribute toward the formation of both of these sounds. In rheumatic carditis, increased intra-auricular pressure as a result of either rapid venous return or mitral regurgitation is a primary cause of both auscultatory phenomena. An easily distendable ventricular musculature as found in the youthful or diseased myocardium is probably of secondary importance. The occurrence of the two sounds in sequence, the order depending on whether the disease process is progressing or regressing, suggests that the murmur probably represents a pathologic extension of the third heart sound. The progression and regression of this series of sounds is well correlated with other signs and symptoms of rheumatic activity.

III. Evaluation of the Third Heart Sound and Early Diastolic Murmur in Rheumatic Carditis.

Clinical interpretation of these sounds in the patient with active rheumatic fever is not an infrequent problem. Many patients are first seen only after a systolic apical blow of mitral insufficiency is well established. In the constant search for evidence of progression or regression of cardiac involvement, special attention to these sounds will often be rewarding. The occurrence of a third heart sound alone cannot, of course, be taken as an outright indication of cardiac derangement, since it is a common finding in the normal child and has an extremely variable and transient nature. However, in the presence of definite evidence of rheumatic activity, the third heart sound assumes a certain amount of added significance. While this sound may possibly have been detectable in the individual patient prior to the onset of the disease state, conditions obtaining in rheumatic carditis add to the factors which favor the appearance of this adventitious sound. The increased intra-auricular pressure resulting from such factors as regurgitation at the mitral valve, an accelerated circulatory mechanism associated with a febrile inflammatory process, and the possible existence of a state of threatened or incipient cardiac failure increase the rate of passage of blood through the auriculo-ventricular valves during early diastole. These factors thus enhance the opportunity for production of the third heart sound. Since information concerning the presence or absence of this sound prior to the disease state is usually not available, there is in those patients who present an apical diastolic third sound on first examination no way of establishing the fact that the third sound is due to rheumatic heart disease. In the great majority of the cases included in this study, however, the third sound appeared while the patient was under observation and can therefore be ascribed to the effects of this disease. Even where the basis of an apical diastolic third heart sound in active rheumatic fever is not clear, the presence of this sound, especially in association with a murmur of mitral insufficiency, should alert the observer to the possibility of the development of an early diastolic murmur. The third heart sound also provides a listening point at which to concentrate attention, since the termination of that sound and the part of diastole which immediately follows it will probably furnish the next definite clue to further progression of the rheumatic process.

The majority of the classical murmurs of rheumatic heart disease, especially the apical systolic murmur of mitral insufficiency and the parasternal diastolic murmur of aortic insufficiency, are generally interpreted as a sign of endocarditis, involving respective valvular leaflets and perhaps the chordae tendinae, although they may in fact be due to myocarditis alone.[20] The existence of pericarditis, on the other hand, can be assumed by the finding of a friction rub and sometimes by characteristic changes in the electrocardiographic tracing. Myocarditis, however, is usually postulated in the presence of endocarditis or pericarditis, since the signs of this lesion are less explicit. Some indication of myocardial involvement can on occasion be derived from changes in the electrocardiogram. However, the few physical signs on which a diagnosis of myocarditis can be based are generally nonspecific, primarily cardiac enlargement or failure and tachycardia. The early diastolic murmur of active rheumatic carditis is particularly valuable as a physical sign in the management of rheumatic carditis since, when it appears, it presents an unequivocal sign of myocarditis as such. The appearance of a third heart sound *de novo* in a patient with active rheumatic carditis is important because it may presage the appearance of an apical diastolic murmur.

Summary

Of 400 children under observation during active rheumatic fever, 115, or 29%, presented either an apical diastolic third sound or an early apical diastolic murmur. Of

these, 54, or 49%, were found to have an apical diastolic third heart sound and an early diastolic apical murmur in some sequence.

The rapid flow of blood from auricles to ventricles during the early diastolic period of the cardiac cycle is thought to be the primary factor responsible for both the third heart sound and the early diastolic murmur. Factors which tend to increase intra-auricular pressure, such as regurgitation at the mitral valve, favor rapid blood flow through the auriculo-ventricular valves and production of these sounds.

The importance of the apical diastolic murmur as a sign of myocarditis *per se* is discussed.

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Spanish Abstract

Sonidos Diastólicos Apicales en Fiebre Reumática Aguda

Durante una investigación clínica sistemática de pacientes con fiebre reumática activa, la interrelación entre el tercer sonido diastólico apical del corazón y el temprano murmullo diastólico se volvieron tan perceptibles que se emprendió un estudio cuantitativo de la relación. De los 400 pacientes con fiebre reumática activa, 115—29%—tuvieron, por lo menos en una ocasión mientras estaban bajo observación, un sonido tercero diastólico del corazón o un murmullo diastólico apical temprano. Un total de 54 pacientes, o aproximadamente la mitad de aquellos que mostraron cualquiera de los sonidos, tuvieron una serie de los dos sonidos durante el período de observación. Las

variaciones de esta serie están en correlación con otra prueba de progresión o regresión del proceso reumático. De este modo, el cambio del tercer sonido del corazón al murmullo ocurrió en el 85% de los casos entre los pacientes gravemente enfermos comparado con el 30% entre pacientes convalescientes, mientras que los porcentajes correspondientes a la transición contraria del murmullo otra vez al tercer sonido del corazón fueron 15 y 70 respectivamente. En cada uno de los pacientes en quien se había observado en un tiempo un temprano murmullo diastólico, había invariablemente presente en el ápice un murmullo sistólico soplante, indicando cierto grado de regurgitación en la válvula mitral.

1740 Bainbridge St.

A COMMENTARY ON NATURAL CHILDBIRTH

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VARIOUS aspects of the rooming-in program from the point of view of the mother, the nurse, and the pediatrician have been emphasized. The obstetricians are no less enthusiastic. Thoms, Jackson and others have shown, after 18 months' experience with mothers in a rooming-in unit, that physically these patients recover as well if not better than those patients not so fortunate as to enjoy an arrangement of this type. Psychologically the advantages are more obvious. The rooming-in mothers have a mental attitude and a morale rarely seen in those mothers who experience the conventional type of hospitalization. That a beneficial mother-child relationship is established in this unit is, we believe, undeniable.

Accepting this as the basic philosophy of rooming-in, it is natural that the obstetrician would come to consider his own role in the furtherance of its establishment. If it is true that the foundations of mental health are laid in infancy and since infancy begins at birth, it seems reasonable to suppose that childbirth itself should be an emotionally satisfactory experience for the mother if an adequate mother-child relationship is to be established. We may question whether childbirth is emotionally satisfactory for most mothers today.

Consider for a moment the course of many pregnancies and labors, particularly in urban areas, today. The woman begins her pregnancy with doubts and fears, many of them founded in ignorance and superstitution, and acquires misinformation from her relatives and friends which contributes to her original anxieties. Despite the reassurance which she receives from her medical attendant as to her physical safety, in his preoccupation with the satisfaction of her somatic needs he may overlook the deep-seated anxieties with which she began her pregnancy and which usually increase as the pregnancy advances. As she nears term, the woman who has had a preconceived idea that labor is a terrifying and dangerous ordeal has experienced little to disillusion her. Assurance that she will be spared pain and suffering by the use of drugs strengthens rather than allays her disquiet.

Such a patient enters the hospital in labor with manifest apprehension and with every expectation of undergoing a traumatic experience. Her attendants, whose interest is often chiefly concerned with her physical safety, may do little at this crucial time to allay her fears. In fact, in assessing many traditional labor room practices in this light, it becomes apparent that their effect is to increase rather than to allay fear. The usage of the word pain as a synonym for uterine contraction, the practice of leaving the patient alone, the routine use of drugs on a schedule rather than according to the patient's needs, the lack of explanation of what is happening, and the often impersonal attitude of the attendants —these and other practices create an atmosphere which may in itself be terrifying.

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Presented at a panel discussion of rooming-in at a meeting of the New England Pediatric Society, New Haven, Conn., June 9, 1948.

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Frequently the patient is partially drugged long before her baby is born and the baby is usually delivered for her while she is unconscious. When the mother does regain consciousness, she often is disinterested in her baby, a disinterest which may last for some time. Is it unreasonable to suppose that such a mother, after a traumatic experience of this kind, could develop an unconscious rejection of her baby incompatible with the establishment of a healthy mother-child relationship? The father, too, relegated to another part of the hospital during the whole process, receiving little more than nonspecific reassurance about something he doesn't understand, is hardly to be blamed if he looks on the newborn as the cause of his wife's suffering and forms conscious and unconscious resentments which may color his relationship to his child for some time to come.

Viewing the process of birth in this light, it is possible that the science of obstetrics, in its concern for the safety of the mother and baby, may have been neglectful of the mother as a personality. Due attention, therefore, should be given to the psychic as well as the somatic needs of the mother, and the goal of modern obstetrics should be to make childbirth an emotionally satisfactory as well as a physically safe experience.

Dr. Grantly Dick Read of London brings this philosophy forcibly to the attention of mothers as well as obstetricians in the book published in this country under the title "Childbirth Without Fear." He suggests that childbirth can be emotionally not only satisfactory but exalting. This is possible since, he points out, fear and its corollary, tension, are the chief causes of pain in normal labor. He demonstrates that by eliminating fear and tension, women can be delivered without undue pain and without the necessity for the use of deep analgesia and anesthesia. He further proposes that the elimination of fear is a more logical approach to the alleviation of pain in childbirth than is the blotting out of consciousness with drugs, which in themselves often complicate an otherwise normal labor and can deprive the mother of an experience to which she is entitled, and from which she and her baby may derive great benefit.

In this clinic our interest in Read's hypothesis and its corroboration in this country by Dr. Blackwell Sawyer, of Toms River, N.J., was further stimulated by several of our clinic patients who asked to have their babies naturally. They had become convinced of the essential truth of Read's ideas by reading his book and were enabled by this alone to achieve their wish for a completely natural childbirth. In the course of a few months approximately 20 of these patients were delivered here, which convinced us that natural childbirth demanded further attention and study.

Consequently, we have been arbitrarily selecting for our program every third patient who registers in our prenatal clinic, provided that these patients are deliverable from below and are not more than 28 weeks pregnant. In this group we include those patients, appearing in ever-increasing numbers, who request natural childbirth.

We attempt, by education, reassurance and constant attendance during labor to eliminate fear insofar as possible and to substitute knowledge and positive emotional values. During the prenatal period these patients receive approximately five short classes in which they are taught the simple physiologic facts concerning pregnancy and labor, exercises designed to improve the function of the trunk and perineal muscles, and some technics of relaxation. These classes are given by the medical and nursing staff of the Department. Patients are encouraged to ask questions and classes are kept on a friendly informal basis. If the patient derives the maximum benefit from these classes, she will enter the hospital when labor begins knowing not only what will happen to her but, also, how she will feel during the labor process. Consequently, she will be calm, confident

and convinced that the experience she is about to undergo is a completely natural one.

In labor these patients are constantly attended by a nurse familiar with the technics of relaxation as well as the philosophy of natural childbirth. The patient is visited frequently by the doctor who will deliver her and kept informed of her progress. If the use of analgesia or anesthesia becomes necessary, the appropriate drugs are administered as indicated. There is no doubt, however, that the institution of the program outlined above minimizes the necessity for the use of medication of this type. During the delivery itself the mothers are kept informed of progress.

If episiotomy is necessary, it is performed after local infiltration of the area to be incised with procaine 0.5% solution. This infiltration is unnecessary in many instances, as the bulging perineum has its own natural anesthesia at the time; however, this natural anesthesia wears off soon after the baby is born and some form of anesthesia is usually necessary for the repair.

As soon as the baby is born the mother usually experiences a profound euphoria, which gives ample evidence of the strong bond which she immediately establishes with her child, and leaves little room for doubt that this is a wholly worth-while procedure. This reaction must be seen to be appreciated to its fullest extent. Third stage bleeding is usually minimal and the expulsion of the placenta is usually prompt. The mother, not having been made sick by an anesthetic, is ready to visit with her husband immediately after leaving the delivery room and her return to normal vigor is prompt.

In addition to the usual hospital obstetric records, we keep complete psychologic records of the pregnancies and labors. We have attempted to classify the labors as successful or unsuccessful. While such a classification has of necessity been arbitrary, it has served a useful purpose in helping us to define our general aims and in enabling us to find at least partial answers to the many questions which natural childbirth poses.

We have considered as successful those mothers who require or receive a minimum amount of analgesia or anesthesia or none at all. All mothers so classified are fully conscious at delivery and have favorable postpartum reactions; that is, they are pleased and happy about their labors and deliveries, and give no evidence of psychic trauma. Those mothers are called unsuccessful who appear to derive no benefit from the indoctrination, who are not conscious at delivery, although they may have received less medication than the usual patient, and whose postpartum reaction is of a negative nature. At the present time we have delivered over 550 women who have been exposed to the technics described above. Our results have convinced us that these technics are physically safe and psychologically desirable for most pregnant women.

SPANISH ABSTRACT

Un Comentario sobre el Parto Natural

Las ventajas psicológicas obvias del plan "rooming-in" hacen que el obstétrico considere los aspectos emocionantes del parto y se pregunte si los dolores del parto y el parto mismo son satisfactoriamente emocionantes para la madre en la cultura de hoy. En el cuidado de la parturienta se ha puesto más énfasis en la satisfacción de sus necesidades somáticas, descuidando amenudo las necesidades psíquicas. Dr. Grantley Dick Read ha indicado que el miedo que existe en la mujer embarazada puede ser la causa del dolor en el parto, y que si se puede quitar este miedo mediante educación y esmerada atención durante el parto, que las mujeres darían a luz sin incomodidad excesiva y sin necesidad de usar analgesia y anestesia en grandes cantidades. Además, estas madres encontrarán que el parto es una experiencia emocionante que satisface.

Se han aplicado la filosofía y las técnicas sugeridas por el Dr. Read a un grupo de pacientes en esta clínica, y hemos encontrado que esto es verdad. Se les da a nuestros pacientes, además del cuidado prenatal, conferencias sobre la anatomía y fisiología del embarazo, dolores de parto, y el parto, yse les enseña algunos ejercicios simples para aumentar su abilidad de relajar. También estos pacientes son atendidos cuidadosamente durante el parto por miembros del cuerpo de médicos y enfermeras. De esta manera un gran número de estas mujeres pueden estar conscientes durante el parto y experimentar la reacción emocionante que satisface tanto y que establece una relación deseable al principio de la vida del infante.

Un análisis estadístico de los resultados de este estudio aparecerá en otra comunicación. Sin embargo, los resultados convencen de que estas técnicas so fisicamente seguras y psicologicamente deseables para la mayor parte de las mujeres embarazadas.

789 Howard Ave.

THE VALUE OF ROOMING-IN EXPERIENCE IN PEDIATRIC TRAINING

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AN experimental four-bed Rooming-in Unit for mothers and newborn babies was inaugurated in 1946 at the Grace-New Haven Community Hospital.[1,2] Accompanying the unit, a rooming-in study group,* including the authors in the position of pediatric fellows, was formed, with the purpose of observing and recording certain factors relating to parent-child relationships in the new-born and infancy period. The time spent as fellows would normally have occupied the second year of pediatric residency training. This type of study program, which Dr. Grover Powers has called the "heart of pediatrics," offers certain unique opportunities and advantages for the training of pediatricians. For the stimulation it may give to the establishment of other such programs, some of the experiences and impressions of the group are recorded.

The main thesis of the study group has been that the separation of mother and baby necessitated under present day hospital and nursery arrangements and the relatively rigid rules of procedure for newborn and infant care and training has led to a denial of certain parental and infant privileges and needs, and that failure to permit natural relationships to develop may be a contributory factor in the development of some of the frequent and important emotional and behavior problems observed in young children. The Unit is an attempt to offer more natural principles of infant care based upon recognition of the individual needs of parents and infants in their relationships to each other.

PROGRAM OF THE FELLOWSHIP

An earlier account of the Unit described its background and physical arrangement, the nature of the prenatal interviews, the selection of mothers and certain procedures.[1,2] The following is a brief description of the work of the pediatrician during his 12 month fellowship.

The close cooperation between the obstetric and pediatric staffs has made it possible for the pediatric fellows to interview mothers in the antenatal clinics. The purpose of the interviews has been fourfold: 1. to select mothers for rooming-in; 2. to obtain background home and family data; 3. to impart information about rooming-in and child care; 4. to establish a continuity of medical supervision for the family. A rewarding by-product of this phase of the work has been an unusual experience in the technic of interviewing. Two psychologists, as well as the director of the study, have served as constant advisers to improve the interviewing of the fellows. A few mothers selected for more detailed study have been given projective psychologic tests prenatally and postnatally, affording the fellows an opportunity to become acquainted with these methods of appraisal.

The selected mothers are observed during labor and followed closely through the rooming-in stay and early posthospital period. The first postnatal interview with the mothers concerns their memories and impressions of labor and delivery. There has been an opportunity of observing many mothers who have experienced natural childbirth according to the method described by Grantly Dick Read.[3,4]

During the mother's eight day stay in the Rooming-in Unit, the pediatric fellows have supervision

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* This group includes the director of the study (Dr. Edith B. Jackson), two psychologists (Dr. Seymour Sarason and Mrs. Elmer H. Potter), the pediatric fellows (the authors), the nursing fellow, and other staff members when special interests are under consideration.

of the baby and, in cooperation wth obstetric and nursing colleagues, guide the breast feeding and breast care. A considerable amount of time is spent in the Unit, which offers the opportunity to observe mother and baby together (and sometimes the father), to make careful note of newborn behaviour, and to answer the many questions which occur to the mothers. A nursing fellow, also a member of the study group, has been invaluable in assisting the pediatricians in answering questions and supplementing observations. One of the fellows is on call at all times. Once a week in the Unit an hour's class for the group of four mothers is used to discuss the care of the newborn baby in the early period at home.

The pediatric fellows are also responsible for the guidance of the pediatric interne working in the regular ward nursery; this responsibility offers a chance to observe larger numbers of babies, to share experience with the interne, and to compare and contrast rooming-in and regular nursery care. A description of this nursery and the type of follow-up made possible by means of home visits has been published elsewhere.[5,6]

More detailed plans for follow-up care and observations are gradually being worked out for a limited number of mothers and babies. The emphasis of the follow-up has changed somewhat. The first fellow (R. W. O.) spent the greatest part of his time working with the neonatal period when the project was just getting under way. The rooming-in babies are now a year older so that the work of the fellows of the second year of the project has broadened to include the older children as well as the new babies coming to rooming-in. Some of the mothers are being followed through a second pregnancy. All mothers and babies (except when distance from the hospital is great) are followed for a period of six weeks by means of weekly home visits. If the mother has a private pediatrician, any follow-up is carried out in close cooperation with him. Night visits or special visits to see sick babies are not possible but the mothers may communicate with one of the fellows by phone any time of day or night and are encouraged to call when they have problems or questions. The Visiting Nurse Association of New Haven, which provides regular home visiting postnatally, is in close working relationship with the fellows, and both communicate by phone concerning problems found during their respective home visits.

The mothers and babies return to the clinic, obstetric and pediatric, respectively, at about six weeks. After this the patients under the care of a private physician are no longer followed closely by the study group; the others are eligible for the Visiting Nurse Association's well baby conferences. The rooming-in fellows are the pediatricians for one of these conferences, meeting twice a week, and the Visiting Nurse Association has permitted a follow-up, in these conferences, of a limited number of rooming-in babies who otherwise would be attending one of the other conferences in the city. This offers a method for continued follow-up of certain mothers and babies. The visiting nurses also send reports of rooming-in babies attending other conferences.

In addition further follow-up is obtained by means of questionnaires and physical, psychologic and developmental examination of the babies at intervals. All of the work of the fellows is directed by means of frequent roundtable discussions with members of the study group.

The fellows also have the medical responsibility for a nearby nursery school offering a chance for observation of older children, some of whom are siblings of rooming-in babies. There is abundant material and time for clinical research on the part of the fellows; in addition, they receive valuable teaching experience, through lectures and classes with parents, nurses, medical students and other staff members. They attend all the regular pediatric staff meetings and so keep in touch with the rest of clinical pediatrics in the department.

In summary, the fellowship offers an opportunity to follow a small number of families in a comprehensive way rather than to see excerpts from the lives of many babies.

The principles of child rearing and child guidance used in this project are those of the permissive method recommended by many pediatricians and child psychiatrists.[7–17] However, it is known that the concepts of this method have not been completely defined or delimited and, even more important, that the flexibility stressed in the method is not alone the answer; the attitudes of the parents, their personalities and the way they feel toward their children play a much greater role in their children's development than does any set of rules of child rearing they may use.

Values

Many of the ideas and attitudes developed in this study during the past year may be the same as those which the majority of practicing pediatricians have, but they represent a divergence from the attitudes of many house staff members on a pediatric service.

Most pediatric training is directed toward the recognition and treatment of disease. What little experience with the newborn or the physically well child it does offer is fragmented and lacks opportunity for follow-up observation. Probably these gaps in training become evident only in practice where the pediatrician must readjust his whole viewpoint. A remarkably large proportion of pediatric practice is concerned with the broad aspects of child health, which is today defined as the physical, mental and emotional well-being of the individual. Rooming-in is an experience unique in pediatric training because it does emphasize this broader definition.

1. Observation of the Newborn

Logically the abnormal is studied in reference to the normal. Therefore knowledge of what constitutes the "normal," healthy individual must be part of the professional equipment of every doctor. Rooming-in gives a year of intensive nursery experience in which close and sustained contact with a varied group of babies is possible.

By direct observation, it was possible to confirm the fact that all babies followed a similar general pattern of development although the timetable of events and the degree of conformity show individual variations.

The quick responsiveness of the babies to their environment, even to apparently insignificant emotional factors was striking. Spontaneous observations, such as that of the mother who remarked that her baby fussed and was dissatisfied at breast only during the few hours when she herself was emotionally upset, have often illustrated the sensitiveness of the baby to his environment within his first week.

The interaction between the baby's individuality and his environment, especially his mother, is further emphasized when the applications and limitations of an ad lib feeding regime are considered. Most babies gradually assume, over a period of weeks and on their own initiative, some semblance of regularity in their feeding and sleeping pattern. Whether or not this feeding pattern is satisfactory depends to a great extent on the type of mother and the amount of stress exerted on her relationship to the baby by other factors in the environment.

2. Problems of Motherhood

The tremendous feeling of responsibility of most new parents and their lack of previous experience with small babies make them particularly defensive and susceptible to feelings of inadequacy if the baby does not seem to be completely happy. The study revealed the importance of helping a mother understand her baby's needs and how to care for them in the way best suited to her capabilities. Because mothers find it difficult to act in a way foreign to their previous education and cultural background, their own ideas about babies and child care had to be considered.

When all the information about the mother, obtained through interviews and observations, was synthesized, the reasons for many problems which might arise and could sometimes prognosticate difficulties became clear. This led to a method of anticipatory guidance found to be reassuring to some mothers. It was usually related to the minor problems of baby care which seem so serious when met for the first time but which assume their proper significance when explained. The frequency of questions about such common occurrences as hiccoughs, constipation, colic, regurgitation, crying and phimosis led to incorporation of advice concerning them in the hospital group discussion.

Among the most important problems of motherhood during the first year is breast feeding. With some doctors its management has become a lost art, in spite of the fact

that many women want to nurse their babies and need help to do so. A lack of knowledge about breast feeding may prevent internes from encouraging it. The problems of nursing are complex and require a certain backlog of experience in order to evaluate fully the intricacies of each feeding situation. Intensive study of breast feeding with detailed observations on many mothers is possible in a rooming-in arrangement where variations in breast routines and, particularly, ad lib feeding may be carried out. One of the assets derived from the year's work has been the confidence gained in helping a mother nurse her baby.

The study has made clear that permissive child care, like any other "system," has its limitations. It cannot be applied in the same way to every mother. Some women need a set of rules for support; others accept the ad lib principles but must modify them to fit their particular family situation. A mother should be encouraged to do what she feels is right as much as possible. Her own judgment about the baby will usually lead her to adopt the method of care most apt to be successful for her. The continuity of contact with the mother and baby has shown that the problems of child care tend to change focus as the child matures, but that the basic relationships maintain their original importance.

3. The Family

In the hospital and, later, at home there was an opportunity to observe the mother and baby, not only as individuals, but also as a part of the family unit. In rooming-in the father has assumed a significant role. The ability of a mother to satisfy and enjoy her baby is directly dependent upon mutual agreement between husband and wife concerning concepts of child rearing and upon harmony in their relationship to each other. Any plans concerning the new baby must be formulated in terms of the other siblings at home. It was learned to appreciate the problems of the private pediatrician in dealing with the complexities of a family situation and to respect his skill in handling them.

4. Child Guidance

The study of the parent-child relationship has naturally and constantly brought contact with the newer concepts of child guidance and their psychiatric bases. One advantage of the fellowship has been the opportunity to test, under expert guidance, the theories learned and to realize their limitations.

At the present time older infants as well as newborns are included in the study. Probblems of the older groups are, for the most part, minor, but some assume a more serious nature and may be termed "behaviour problems." In the well baby conference where the history, personality structures and relationships of the family constellation were all known, the evolution of some of these problems was clear. If the kind of difficulty which develops into a severe behaviour problem is recognized early enough, the pediatrician can sometimes arrest its development before it becomes serious enough to require the aid of a psychiatrist. Because this kind of preventive treatment requires insight into the mechanism of behaviour disorders and respect for their potential gravity, caution in attempting to treat such delicate situations has been found essential.

Conclusion

Rooming-in fellowship has been a fruitful period in which practical experience, research facilities and teaching opportunity have been well blended. This type of training

combination is maximally effective only if there is a stable, directive nucleus to the study group which serves to orient the fellows and guide their research plan.

Because of its emphasis upon the understanding of the total individual, rooming-in has fostered a more mature and sympathetic insight into the patient. The more one learns of behaviour, the more one is willing to accept deviations and to try to understand their causes. This consideration of the individual, with his own cultural milieu, family background and personal experience, will broaden our pediatric approach.

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Spanish Abstract

El Valor de la Experiencia "Rooming-In" en la Enseñanza Pediátrica

Una Unidad "Rooming-In" fué inaugurada en el Servicio de la Universidad en el Grace-New Haven Community Hospital en 1946, y se formó un grupo de estudio en conjunción con la Unidad para estudiar las relaciones entre las madres y los niños durante el período del nacimiento y de la infancia. Los autores describen el valor de su experiencia como una parte del programa de enseñanza pediátrica de residencia.

Se ha hecho un estudio de cerca de los recien-nacidos y sus familias mediante entrevistas prenatales, observaciones de crianza en la Unidad "Rooming-In" y frecuentes visitas a sus casas. Se da énfasis al método permisivo del cuidad de niño, y se fomenta la alimentación de pecho.

Los autores creen que a causa del énfasis que se les ha dado a los aspectos de la salud del niño, incluyendo el bienestar físico, sentimental y mental, y el entendimiento del inviduo en general, su acercamiento pediátrico se ha ensanchado. Ellos recomiendan fuertemente el establecimiento de estas oportunidades de enseñanza, y dan énfasis a la necesidad de un nucleo estable de grupos de estudio similares.

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CHANGE IN THIOCYANATE AND SODIUM^{24} SPACES DURING GROWTH

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IT IS generally agreed that the water content of the body decreases during growth. Direct evidence stems for the most part from desiccation studies and tissue electrolyte analyses in experimental animals.[1-3] More recently, direct measurement of spaces occupied by different substances which have an extracellular distribution has been accomplished in the intact individual. The availability of radioactive isotopes of sodium and chloride has permitted measurement of the distribution of these ions when the amounts injected were so small as not to alter the previously existing electrolyte pattern. Thiocyanate has also been employed as a measure of extracellular fluid and while its distribution is not wholly extracellular, the extremely slow rate of excretion makes it more satisfactory than nonmetabolized carbohydrates such as inulin, mannitol and sucrose. Application of such space measurements has supported the idea that there is a decrease in body water, especially in the extracellular fluid compartment, during growth. The thiocyanate space[4-6] has been measured in children of various ages excluding very young infants, and the space occupied by sodium^{24} has been reported in three newborn infants.[7]

In approaching this problem it seemed wise to study subjects ranging from premature infants to adults and to make simultaneous measurements of changes during growth in the spaces occupied by a number of different substances presumed to measure the extracellular fluid compartment. Demonstration of parallel changes in the spaces occupied by these different substances would strengthen the supposition that such changes reflect real variations in the specific fluid volume, rather than alterations in the distribution of the substances between different fluid compartments. Substances of choice for this purpose should include both electrolytes and nonelectrolytes, since it seems unlikely that parallel changes in the spaces occupied by these two types of substances could be due to exactly comparable alterations in distribution. For these reasons we made concurrent measurements of the space occupied by thiocyanate, sodium^{24}, inulin and mannitol at ages from prematurity to adulthood.

PROCEDURE

Forty determinations were made on 36 subjects, including three premature infants and five adults. All were free from known kidney disease or body fluid disturbance. The analyses were made at least

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2½ hours after ingestion of customary diets in an air-conditioned metabolism unit in which the temperature and humidity were maintained at 26° C. and 60%, respectively.

One or more of the four substances, thiocyanate, sodium^{24}*, inulin and mannitol, were injected simultaneously by a previously described quantitative method for the intravenous injection of small volumes of fluid[8] in the following dosages:

5% thiocyanate	0.5 ml./kg.
sodium^{24}	2 microcurie/kg., up to a maximum of 100 mc.
10% inulin	2.0 ml./kg., up to 100 ml.
25% mannitol	1.0 ml./kg., up to 50 ml.

Blood samples were drawn and urine samples collected before and at intervals following the injection.

In younger subjects, urines were collected through an indwelling catheter, and the bladder completely emptied by blowing out with air.[9] In older subjects, spontaneous voidings at the required times were employed.

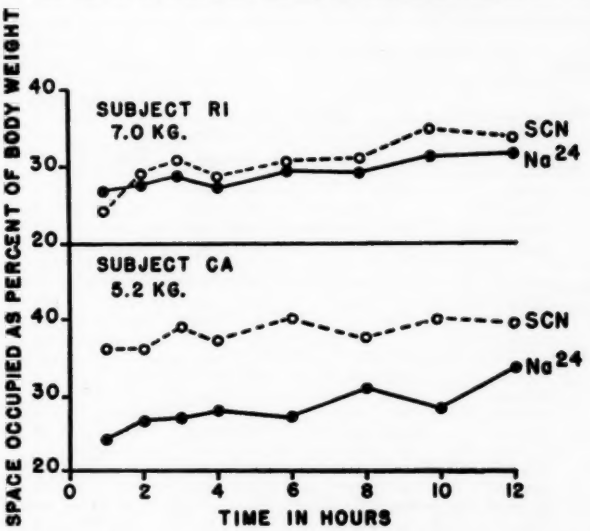

FIG. 1. Variations in space occupied in infants by sodium^{24} and thiocyanate during 12 hour periods following injection.

Chemical and isotope counting methods: Thiocyanate was determined in plasma and urine by the method of Crandall and Anderson as modified by Lavietes et al.;[10] inulin by a modification of the method of Hubbard and Loomis;[11] and mannitol by the method of Corcoran and Page.[12] All determinations were done in duplicate and a calibration curve was run with each group of unknowns, a reagent blank being used for the center setting. In the earlier studies the gamma activity of sodium^{24} was counted in a total volume of 50 ml. containing 1 ml. of serum or 1 to 25 ml. of urine diluted with water.† Later, beta activity was counted with a single end-window Geiger counter after drying 1 ml. samples of serum and 1 to 5 ml. samples of urine for ½ to 1 hour at 105° C.

Calculations: The spaces occupied by the various substances at a given time following injection were calculated from the formula:

* Sodium^{24} was obtained from the Columbia University Cyclotron Laboratory through the courtesy of Professor John Dunning; it was standardized in the Radiological Research Laboratory, College of Physicians and Surgeons, through the courtesy of Dr. Edith Quimby.

† This counting was done in a tube with exceptionally high gamma sensitivity specially designed by the Texas Co. The measurements were made in the biophysics department of the Sloan-Kettering Institute by Ruth S. Hill.

Space occupied = (amount injected − amount excreted)/serum concentration

The data were calculated in this uncorrected form in agreement with the reasoning of Gregersen and Stewart[13] and, following its use, by Kaltreider et al.[14] and Morse et al.[5]

To compare the constancy of distribution in infants with that reported in adults,[14] observations were made on 11 infants ranging in age and weight from 2½ to 42 weeks and from 3.18 to 7.9 kg., respectively. Following the injections of thiocyanate and sodium[24], blood and urine samples were collected at frequent intervals over a 12 hour period and spaces calculated from these data. Two representative series of observations are shown in Figure 1. In general, the results are similar to those

TABLE I

REPRESENTATIVE PROTOCOLS AND RESULTS OF SPACES OCCUPIED BY THIOCYANATE, SODIUM[24], MANNITOL AND INULIN IN FOUR SUBJECTS

Subject	Substance	Space Occupied as Per Cent of Body Weight: Time after injection hours						Urinary Excretion Cumulative Percentage: Time after injection hours		Serum Protein gm./100 ml.
		½	1	1½	2	2½	4	2½	4	
Baby F.L., female	NaSCN		40.1			40.8	40.9	0.9	1.3	5.69
Age 1 wk.	Sodium[24]			47.1		48.3	51.6	0.6	0.7	
Wt. 3.24 kg.	Mannitol		44.7	45.4	47.5	48.5	58.2	37.1	46.6	
	Inulin		40.4	43.8	53.4	49.1	66.1	44.2	51.0	
Baby R.A., male	NaSCN			30.9		31.3	31.1	1.0	1.6	6.40
Age 9 mos.	Sodium[24]			32.0		34.7	36.9	1.3	1.9	
Wt. 9.85 kg.	Mannitol			33.6		40.2	42.9	72.7	86.8	
	Inulin			27.3		27.8	25.0	87.9	96.7	
M.A., male	NaSCN		23.9	24.7		24.9	25.0	0.8	1.2	8.0
Age 9½ yrs.	Sodium[24]		25.9	27.4		28.1	28.3	0.3	0.4	
Wt. 36.9 kg.	Mannitol		26.2	36.9		47.9	72.7	60.2	70.5	
	Inulin		27.1	30.0		45.2	57.7	83.3	88.8	
H.E., male	NaSCN	22.3	22.8	23.0	23.1	22.8	22.7	0.7	0.9	7.98
Age 26 yrs.	Sodium[24]	25.1	24.7	25.7	26.7	27.3	28.0	0.6	0.8	
Wt. 58.0 kg.	Mannitol	23.0	23.2	26.0	29.1	27.9	67.8	52.5	63.1	
	Inulin	16.9	20.9	22.2	25.7	28.9	32.8	71.2	79.7	

found in adults over a period of 12 hours, although the range of variation was too great to detect the increase of sodium[24] space over thiocyanate space at 12 hours reported in adults.[14] Reasonably stable distribution was attained in all instances by two hours after injection. In subsequent observations, therefore, although two or more blood samples were drawn following each injection, calculated spaces occupied between 2½ and 4 hours after injection were utilized for comparison.

RESULTS

Representative protocols and results for four subjects are shown in Table I. These examples are characteristic of 11 series of observations during which thiocyanate, sodium[24], mannitol and inulin spaces were determined simultaneously. It is apparent from these examples that, under the conditions of these experiments, both inulin and mannitol spaces continued to increase with time following injection and never reached a constant value. A graphic description of two such series of observations is shown in Figure 2. Thiocyanate and sodium[24] are both slowly excreted whereas both mannitol and inulin are rapidly excreted as shown by the cumulative percentage excretions in Table I. It seemed possible, because of the constancy of the space occupied by thiocyanate and sodium[24], that failure of the mannitol and inulin spaces to reach constant values might be due to a cumulative error of large magnitude in the calculations of the amount of the carbohydrates excreted. This could produce a progressive increase in the value calculated for the space occupied. To evaluate this source of error, experiments were performed on dogs, first under circumstances comparable to those in human subjects and then after ligation of the renal pedicle. In the latter, errors from urinary loss were excluded.

Results in one normal dog and in two dogs with ligated renal pedicles are shown in Figure 3. It can be seen that after ligation the space occupied by inulin remained constant whereas the mannitol space continued to increase, though less than in the intact dog. Progressive increase in the mannitol space in the absence of renal loss may be due to slow metabolism of the substance as suggested by Dominguez et al.[15] These results in dogs together with the occasional finding of constant inulin spaces in subjects when complete recovery of inulin was obtained suggest that better urine collections would permit the determination of a reproducible inulin space in intact individuals. This would not be expected, however, with mannitol.

It is notable in the two experiments on dogs with renal pedicles ligated that the spaces occupied

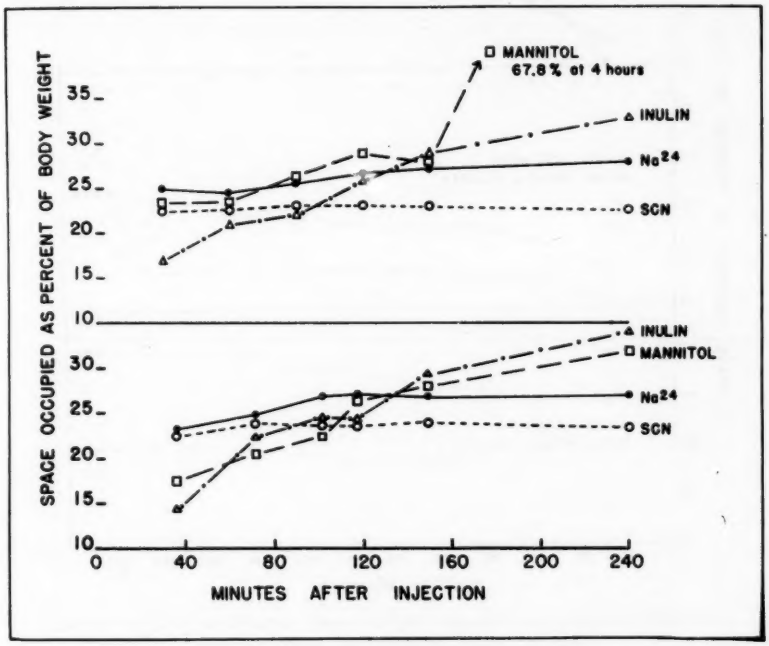

FIG. 2. Changes in relationships between spaces occupied by thiocyanate and sodium^{24}, and by mannitol and inulin, with time following injection.

by the three different substances differ markedly but in a consistent order: the space occupied by inulin is less than 20% of the body weight; that by mannitol around 25%; and that by thiocyanate around 35%.

There is no physiologic justification for assigning any significance to the increasing spaces occupied by mannitol and inulin at the time, about two hours after injection, when they happen to be in the same range of values as the constant spaces occupied by thiocyanate and sodium^{24}. For this reason we believe that under the conditions of the observations in our human subjects, no conclusions can be drawn concerning spaces occupied by these two nonelectrolytes.

Changes in spaces occupied by thiocyanate and sodium^{24} on the other hand are significant. Values for 36 subjects are shown in the scatter diagram of Figure 4, and average values for subjects of different weight ranges are given in Table II. It can be seen from these data that as growth proceeds there is a definite over-all decrease in the spaces occupied by both substances when expressed as per cent of body weight. Secondly, the wide range of values for both sets of data apparent in infants decreased markedly in the adults. Finally, there is relatively little variation in values between the 5.2 to 10.7 kg. and the 19.8 to 23.3 kg. group. Most of the over-all decrease occurs in early infancy

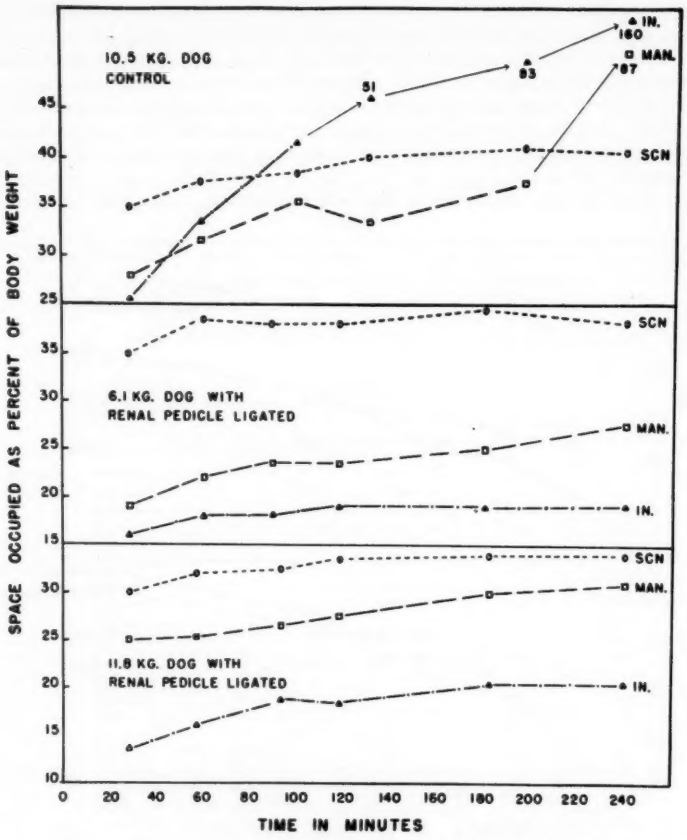

FIG. 3. Variations in spaces occupied by thiocyanate, mannitol and inulin in control dog and in two dogs with renal pedicles ligated.

TABLE II

NUMBER OF OBSERVATIONS AND MEAN VALUES FOR THIOCYANATE AND SODIUM^{24} SPACES FOR SUBJECTS GROUPED ACCORDING TO WEIGHT

Weight kg.	NaSCN Space			Na^{24} Space		
	Number of observations	Per cent of body weight		Number of observations	Per cent of body weight	
		Mean	Range		Mean	Range
2.1– 4.8	16	41.2	36.6–45.9	15	42.6	31.0–51.8
5.2–10.7	14	35.0	27.3–39.8	13	33.0	29.6–42.7
19.8–23.3	4	32.2	28.3–34.6	4	35.6	31.9–39.0
Adults	4	23.1	21.9–23.8	5	27.1	25.3–27.9

with a definite though smaller decrease as adulthood is approached. These findings are in agreement with those[5] in which no marked change in thiocyanate space calculated as per cent of body weight was found in children ranging from three to 17 years of age. They similarly agree with the finding of sodium[24] spaces of 43% of the body weight in newborn infants[7] as contrasted with an average value of 24.7% found in adults.[14]

Comment

Our calculations of fluid space in man are limited to the data obtained with the two electrolytes, thiocyanate and sodium,[24] because only under the experimental conditions excluding renal excretion in dogs and in the occasional subject where complete recovery

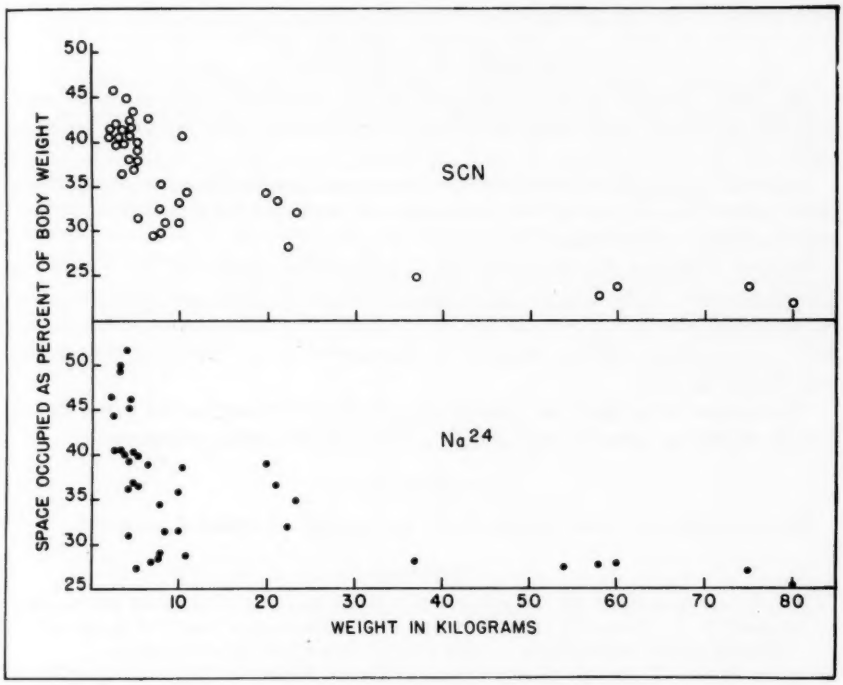

FIG. 4. Values for spaces occupied by thiocyanate and sodium[24] in subjects ranging in weight from 2.1 to 80 Kg.

of inulin was accomplished did inulin attain a constant space. This was not true of mannitol under any circumstances. Our human subjects were all in good health with no evidence of impaired renal function and there has been no opportunity to observe the distribution of these carbohydrates in clinical cases of anuria. We hesitate to relate the spaces occupied by thiocyanate and sodium[24] to extracellular fluid volume, since, judging from data on chloride space,[16] the extracellular fluid volume is probably smaller than the spaces occupied by either Na or thiocyanate. It is not even certain that the observed changes during growth reflect changes in the extracellular fluid volume, but parallel decreases in the space occupied by two different substances support the introductory supposition that they reflect comparable changes in a specific fluid space rather than exactly equal alterations in distribution between different fluid compartments.

If changes in the spaces occupied by these two substances do reflect corresponding changes in extracellular fluid volume, they indicate that the young infant has an extracellular volume expressed as per cent of body weight which is 57 (sodium^{24}) to 78 (thiocyanate) % greater than that of the adult. These differences, although considerably greater than generally considered, are not incompatible with estimates made by other methods.[3] Finally, these findings show that the decrease during growth in the space occupied by thiocyanate and sodium^{24}, whether due to a decrease in extracellular fluid volume or to a change in distribution of the two substances, occurs at two distinct periods of growth. There is a rapid decrease during early infancy and a smaller decrease during adolescence with an intervening period of relative constancy.

Summary and Conclusions

The spaces occupied by one or more of the four substances, thiocyanate, sodium^{24}, mannitol and inulin, were determined in 36 subjects ranging from premature infants to adults.

No conclusions could be drawn concerning the spaces occupied by mannitol and inulin, since, under the conditions of the observations in our human subjects, neither of these spaces reached a constant value.

There is a definite decrease in the spaces occupied by thiocyanate and sodium^{24} as growth proceeds. If the changes in the spaces occupied by these two substances reflect corresponding changes in extracellular fluid volume, they indicate that young infants have an extracellular volume which is 57 (sodium^{24}) to 78 (thiocyanate)% greater than that of the adult.

The decrease in the spaces occupied by thiocyanate and sodium^{24} occurs at two distinct periods of growth: primarily during early infancy and also during adolescence.

Acknowledgment

We are indebted to Flora Hurwitz, R.N., for nursing and technical assistance.

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SPANISH ABSTRACT

Cambios en los Espacios de Tiocianato y Sodio^{24} durante el Crecimiento

Los espacios ocupados por uno o más de las cuatro sustancias, tiocianato, sodio^{24}, manitol e inulina, fueron determinados en 36 sujetos—de infantes prematuros a adultos. No se pudo llegar a ninguna conclusión con respecto a los espacios ocupados por el manitol y la inulina, ya que ninguno de estos espacios alcanzó valor constante en nuestros sujetos humanos bajo las condiciones de observación. Hay una disminución marcada en los espacios ocupados por el tiocianato y el sodio^{24} a medida que el crecimiento adelanta. Si los cambios en los espacios ocupados por estas dos sustancias refleja cambios correspondientes en el volumen de flúido extra-celular que es 57% (sodio^{24}) a 78% (tiocianato) mayor que el del adulto. Ocurre disminución en los espacios ocupados por el tiocianato y el sodio^{24} a dos períodos distintos de crecimiento—durante la temprana infancia y también durante la adolescencia.

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THE CHANGED STATUS OF DIPHTHERIA IMMUNITY

By PHILIP COHEN, M.D., HERMAN SCHNECK, M.D., EMANUEL DUBOW, M.D., AND SIDNEY Q. COHLAN, M.D.
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THE morbidity and mortality rates of diphtheria in various sections of this and other nations have been increasing for the past several years. The incidence of diphtheria is dependent upon the prevalence and virulence of C. diphtheriae and the immunity of the population. Immunity is a composition of age, race and climate, and also local, cellular, tissue and humoral immunity.[1,2] The latter two, which are the more important factors in determining ultimate immunity in our climate, are controllable and remediable. It is the cellular and humoral phases of immunity and their changed status in the past generation, already gaining recognition, which is of concern in this study.

Analysis of the data compiled by Schick[1] in Vienna and New York showed that in the period 1914 to 1923, 86% of the adults were immune to diphtheria and that this immunity was transmitted to the babies born of that generation.

Zingher,[3] in 1923, published the results of Schick tests on more than 150,000 children in New York schools. Although the majority of these nonimmunized children gave a positive Schick test upon entering school, 82% were Schick negative at 16 years of age. The percentage of positive reactions diminished rapidly after the age of seven years.

At this time prophylactic active immunization against diphtheria was undertaken with significant changes. A decline in the diphtheria case and death rates resulted, and case rates of less than 1% of former figures were reported in many sections of the country.[4] This decrease was accompanied by a considerable decline in the carrier rates in the communities carrying out artificial active immunization and therefore a decline in the opportunity to develop an immunity from naturally acquired stimuli. This in turn was related, apparently, to a widely noted decrease in the general level of immunity in many sections of the population. Schick test surveys for immunity to diphtheria among young adults in this country as well as in England, Canada, Australia, Norway and other countries have shown that 50 to 70% of the population are susceptible to diphtheria even in epidemic areas,[5–23] in contrast to the incidence of 15 to 20% of susceptible subjects reported formerly in this age group.[12–13] Wright and Clarke[22] found that 51.6% of 250 postpartum women had positive Schick reactions and that over half the infants of these mothers had positive reactions. (See Table I.)

Accompanying the increased adult susceptibility to diphtheria, numerous outbreaks and epidemics of this disease have been reported in different parts of the world, and a progressive increase in the case rates has occurred since 1941.[4] While epidemics in Norway, Holland, Germany and Sweden may be attributed to lack of mass immunization, this explanation does not apply to outbreaks of diphtheria in immunized communities in

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TABLE I

DIPHTHERIA IMMUNITY IN ADULTS (1932–1944)*

Authors	Date	Region	Number of cases	Age Group Yrs.	Schick positive
Cooke and Sharma[42]	1932	St. Louis	643	30	30
Liebling et al.[47]	1941	Chicago	—	25	52.8
Campbell[20]	1941	Halifax	405	20	59
	1941	Halifax	243	18	80
	1941	Halifax	250	25	55
	1941	Halifax	—	22	71
	1941	Halifax	558	(Adult)	87
Wishart[21]	1943	Canada	72	20	52.7
Karelitz and Moloshok[10]	1944	Americans in Africa	1283	20–25	28.6
Wright and Clarke[22]	1944	London	250	28	51.8
Bull U. S. Army[26]	1944	U. S.	2933	20–30	44
Cohen et al.[43,45]	1946	New York City	175	18–35	52

* From Cohen and Scadron.[44–45]

Canada and England[24] and in this country.[25] Diphtheria was a real problem in American overseas armies.[26,27] In diverse sections of this country including New York City,[28,29] there has been a rise of diphtheria cases since 1945. These cases have been almost evenly distributed among the age groups of 1 to 5, 5 to 10, and above 10 (Table II), and have occurred for the most part in individuals previously immunized.

TABLE II

DIPHTHERIA IN NEW YORK—1947

Age	Cases	Deaths
Under 1	14	1
1	15	
2	33	3
3	29	1
4	41	
5– 9	115	2
10–14	48	3
15–19	13	
20–24	15	
25–34	20	
35–44	16	2
45–Over	19	
Total	378	12

The young adult population has borne the brunt of these epidemics.[30] This is because artificial immunity wanes rapidly within a few years. Fraser and Halpern and others[31–33] showed that three months after immunization with three doses of fluid toxoid a large number of previously susceptible children had over .02 unit of antitoxin per cc. of serum,

TABLE III

DURATION OF DIPHTHERIA IMMUNITY*

Interval after immunization	% Schick positive
6 mo.	0.4
1 yr.	3
3 yr.	8
5 yr.	34

* From Cohen and Scadron.[44-45]

a figure more than adequate for the production of a negative Schick test.[1,34-36] After one year, 3% showed positive Schick tests (Table III). The percentage then increased rapidly so that at the end of five years almost 35% of the immunized group were Schick positive, and the average serum antitoxin titer was only 20% of the maximum obtained shortly after immunization.[37] In a recent study it was found that the relapse rate may be as high as 20% in one year.[38] Fraser has also shown that 10 to 18 years after primary immunization, 50% of a group of women had less than .01 u./cc. serum of antitoxin and consequently gave positive Schick reactions.[39]

Since there is ample evidence that the majority of adults in many areas of the country are susceptible to diphtheria, the immunity attributed to the newborn baby may often rest upon false assumption. In 106 cases of diphtheria in infancy reported in two large cities in Norway[40] there were 11 deaths in the 76 infants under six months of age. Robin and Brunel in France[41] reported two epidemics of diphtheritic coryza which occurred in the maternity ward. Twenty-six nursing infants were affected and there were eight deaths.

In view of such findings, Schick tests were performed on 683 women (pregnant and nonpregnant) and also on the babies delivered of the pregnant women. All the Schick tests were interpreted by one or more of the authors. The total of 274 Schick positive cases were graded according to standard accepted criteria. The intensity of the reactions were classified as either 4+, 3+, 2+ or 1+ (Table IV).

Of 683 controlled Schick tests a total of 274 (40.1%) were positive and 409 (59.9%) were negative. The figures according to age group are shown in Table V.

Of the 91 additional cases from the private practice of one of us (P.C.), a total of 62 (68.1%) were Schick positive and 29 (31.9%) were Schick negative. The difference in percentages of Schick positive reactions in these two groups is readily apparent. There appeared to be little difference in distribution of adult diphtheria immunity, as measured by the Schick test, between the foreign born and the low income U.S. born group living in New York's lower East Side.

TABLE IV

INTENSITY OF SCHICK REACTIONS IN MOTHERS

Schick	4+	3+	2+	1+	Total
Number	97	62	76	39	274
% of total	35.5	22.6	27.7	14.2	

TABLE V

SCHICK REACTIONS ACCORDING TO AGE GROUPS

Age	No. Pos.	% Pos.	Totals
17–25	96	41.0	234
26–30	102	41.1	248
31–35	45	36.0	125
36–45	25	36.8	68
Unknown	6	75.0	8
Totals	274		683

The results of the relationship to previous immunization in 434 cases taken from the above clinic and private groups are recorded in Table VI.

The percentage of patients with previous immunizations was almost the same in both Schick positive and Schick negative groups. In the private cases, the percentage of patients who had previous immunization was much higher, but again the ratio was the same between the Schick positive and the Schick negative reactors. This finding appears to indicate that childhood immunization has little effect on the immunity of an adult population. These data confirm the findings of Fraser and Brandon[37] that active immunization is largely lost within a few years unless booster injections are given.

A group of 57 Schick positive mothers, selected from the original 683 women, and their newborn infants, were studied for comparative Schick reactions. The ages of the children ranged from three weeks to six months. Each mother and her own child were Schick tested and readings were made simultaneously four days later. Results are shown in Table VII.

It is apparent that the intensity of the skin reaction in the children is much decreased as compared to the mothers. The latter show a great preponderance of 4+ reactions (61.4%).

Among the children, a 4+ reaction is unusual (3.5%), and almost half of the children of Schick positive mothers had negative skin reactions. Grouping the children by age would show more clearly the decreased reactivity of the infant's as compared to the mother's skin, and a tendency toward increasing skin reactivity in children in older months.

A group of 98 mothers, also taken from the original 683 cases, and their infants was

TABLE VI

SCHICK REACTIONS IN RELATION TO PERVIOUS IMMUNIZATION

	Schick Positive			Schick Negative		
	Total	Prev. immun.	%	Total	Prev. immun.	%
Clinic cases	131	77	58.8	225	132	58.6
Private cases	51	43	84.3	27	22	81.5

TABLE VII

INTENSITY OF SCHICK TESTS IN SCHICK POSITIVE MOTHERS AND INFANTS

	Mother		Child	
	Number	%	Number	%
4+	35	61.4	2	3.5
3+	5	8.8	3	5.3
2+	12	21.0	11	19.3
1+	5	8.8	14	24.5
Neg.	0	0.0	27	47.4
Totals	57		57	

tested within the first few days postpartum with the following results: 54 of the mothers were Schick positive and 44 were Schick negative. Only seven babies (13%) of the 54 Schick positive mothers were Schick positive. Other investigators[22,42] have demonstrated a similar anergy to Schick test toxin in the skin of newborn infants. In order to show that the apparently negative Schick test was not due to immunity of the newborn, blood titration studies for diphtheria antitoxin (by the method of Frobisher) were done on maternal blood taken on delivery and on cord blood, representing the fetal circulation. Results and their correlation with the Schick test are shown in Table VIII.

TABLE VIII

COMPARISON OF SCHICK TESTS AND BLOOD ANTITOXIN TITERS OF MOTHERS AND NEWBORNS

Case	Schick reaction mother	Blood diph. antitoxin titer mother	Schick reaction baby	Blood titer baby
1. E.S.	++++	0.01−*	+	0.01−
2. L.M.	++++	0.01−	neg.	0.01−
3. R.K.	++	0.01+	neg.	0.01−
4. H.S.	++	not reported	neg.	0.01−
5. S.S.	++++	0.01−	+	0.01−
6. R.G.	+++	0.01−	+	0.01−
7. V.N.	+++	0.01−	neg.	0.01−
8. A.C.	+++	0.01−	neg.	0.01−
9. A.S.	++	0.01−	neg.	0.01−

* Less than 0.01 u/cc. serum diphtheria antitoxin.

COMMENT

Our data showed that more than 40% of 683 adult females from various sections of New York City are Schick positive. Antitoxin titrations have corroborated the findings that the great majority of the Schick positive women have less than 0.01 u./cc. serum of diphtheria antitoxin indicating susceptibility to diphtheria.

Analysis of the whole series reveals that previous childhood immunization seemed to exert no effect upon the adult status of immunity to diphtheria.[39] Childhood attacks of

diphtheria also apparently had little or no effect upon the Schick test of the adult, either because antitoxin had been administered or the active immunity had been lost with the passage of years. The percentage of positive Schick tests in foreign born and native born was approximately the same.

Anergy of the young infants' skin to diphtheria toxin, noted by previous observers,[1] was confirmed by this study. Since the circulating antitoxin content is the same in mother and baby, it may be inferred that a negative Schick test in the newborn is not a reliable criterion of immunity. The babies of a group of 57 Schick positive mothers, shown in Table VII, were tested to determine the duration of this anergy. Nearly half of the younger infants of Schick positive mothers were Schick negative, and the others, with two exceptions, showed less intense reactions than their mothers. We have come to learn that the Shick test of the mother is a much more reliable test of the infant's immunity to diphtheria than the baby's own reaction.

It is probable that some 40 to 50% of the adult population in New York City and other sections of the country are Schick positive and lacking an adequate protective amount of circulating antitoxin. There are diverse factors determining ultimate immunity and disease incidence in diphtheria, but humoral immunity and cellular immunity play a major role.

The customary procedure at present is to start active immunization in infancy and early childhood after which little is done to maintain immunity. From these studies, it is learned that with this procedure a great proportion of the adult population lacks humoral immunity, and is hence more susceptible to diphtheria under certain conditions, as are their newborn infants. This raises the question, is it advisable to follow the usual policy of doing nothing until diphtheria strikes a community and then institute or reinstitute mass prophylaxis, as is the usual procedure in smallpox epidemics? Or would it be a better practice to maintain periodic recall injections, particularly in the female during the childbearing period? Maternal immunization with resulting passive immunity of the newborn has been described and is now favored in the form of combined immunization.[43–45]

In the event that maternal immunization is not utilized there remains a second method to protect the infant. This method is to determine the immunity of the mother during pregnancy to learn whether the newborn baby will be immune. If the mother shows no signs of immunity, immunization of the baby is begun at two months of age, for there is no blocking of antitoxin formation by preformed antitoxin if the maternal and hence the infantile antitoxin is low. If the mother is immune, either naturally or through immunization during pregnancy, active immunization of the baby is begun at four months of age, when studies have shown that the infant has largely lost its transferred passive immunity. At this age antigenic stimuli may be more effective. Since the newborn baby has little immunity to pertussis,[44–46] it has been our policy to use a combined vaccine. This selective immunization of infants, judging their immune status by a study of the maternal immunity, would seem to remedy the infants' immunologic deficiencies at the earliest desirable opportunity. Preparations of combined toxoid (diphtheria and tetanus) and pertussis bacilli vaccine of adequate dosage are now available, so that three injections at monthly intervals in dosage indicated for uncombined diphtheria toxoid promises to achieve immunity against all these infections.

Summary

These studies and data indicate a considerable diminution of immunity to diphtheria among the present young adult generation of this city. The same seems to hold true for

other sections of this country. While the increase of diphtheria morbidity has not been alarming in this country, it is not wise or expedient to delay the correction of this lost or waning immunity until diphtheria assumes threatening epidemic proportions. Since the soil may be prepared for the spread of diphtheria by loss of humoral immunity, a change in one of the other factors affecting the epidemiology of this disease may effect a sudden and serious increase of diphtheria. The validity of the Schick test has been reestablished as an index of humoral immunity by once more demonstrating its close correlation with an adequate antitoxin content of the blood. The reliability of the Schick test, since it is simple, easy to perform and interpret and always available, is stressed.

The restoration of humoral immunity to diphtheria and the excitation of cellular immunity by periodic stimulating inoculations will cause a decline in diphtheria susceptibility and morbidity. These ends can be attained by continuing, during childhood and early adult life, recall doses at periodic intervals, thus converting the potential protection of cellular immunity into the active protection of the humoral immunity. In the case of women it may be wise to increase such immunity to an adequate level during pregnancy to safeguard the newborn with similarly adequate immunity.

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SPANISH ABSTRACT

El Estado Cambiado de la Inmunidad de la Difteria

Nuestros estudios e informes indican una disminución considerable de inmunidad a la difteria en la última generación en la Ciudad de Nueva York. Lo mismo ha ocurrido en otras partes de este

país. Aunque el aumento de morbidad de difteria no ha sido generalmente de alamarse en este país, no creemos conveniente posponer la correción de esta inmunidad perdida hasta que la difteria llegue a proporciones amenazantes o cause epidemia. Como el terreno puede estar preparado para el esparcimiento de difteria mediante la pérdida de inmunidad humoral, un cambio en uno de los otros factores que afectan la epidemiología de esta enfermedad puede efectuar un aumento de difteria serio y repentino. Hemos restablecido la validez del ensayo de Schick como un índice de inmunidad humoral demostrando una vez más su estrecha correlación con un contenido de la sangre antitoxino adecuado. Acentuamos la confianza o seguridad del ensayo Schick ya que es simple, fácil de hacer y de interpretar, y está siempre disponible.

Creemos que el restablecimiento de la inmunidad humoral a la difteria y la excitación de inmunidad celular mediante inoculaciones estimulantes periódicas causarán una decadencia en la susceptibilidad y morbidad de difteria. Esto se puede hacer continuando con dosis de recordación periódicas a intervalos de tres a cinco años durante la niñez y vida adulta temprana, convirtiendo la protección potencial de inmunidad celular en protección activa de inmunidad humoral. Es prudente aumentar tal inmunidad a un nivel adecuado durante el embarazo para proteger al recién nacido.

1175 Park Avenue

PENICILLIN TREATMENT OF DIPHTHERIA CARRIERS

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IT HAS been reported[1] previously that penicillin shortens the period of the carrier state both for cases of acute faucial diphtheria as well as for convalescent and chronic carriers. In a comparison of results in 80 penicillin-antitoxin treated cases of acute faucial diphtheria with 42 control cases of acute faucial diphtheria treated with antitoxin alone, Karelitz et al. made the following observations. At five days after onset of acute faucial diphtheria, the percentage of positive throat cultures among the penicillin treated patients was 27.5% against 100% for 42 controls; at 10 days, positive nose and throat cultures were obtained for 7.5% and 92%, respectively. At 15 days, less than 5% of the penicillin treated patients remained positive against 85.7% for the controls. Local therapy in the form of nose drops or nasal spray of a solution of penicillin 1,000 u./ml. in physiologic saline was ineffective in most cases, even when the treatment was continued for 21 days.

The literature on the subject of penicillin treatment of diphtheria carriers has grown in the past two years,[2-7] and the preponderance of evidence indicates that penicillin is effective in eradicating C. diphtheriae. Yet opinions are not uniform as to dosage and duration of penicillin treatment and the route of administration which yield best results.

Several studies have been projected to answer these questions. The purpose of the first was to see how quickly C. diphtheriae could be cleared from the nose and throat of carriers by intensive therapy, such as the combined use of intramuscular penicillin and penicillin nose drops. The dosage of penicillin previously employed[1] and found adequate for most adult carriers and cases of faucial diphtheria was 15,000 to 25,000 u. every three hours. Larger doses were not used because of the limited supply of penicillin made available for the study at the time. The failure of some patients to respond to these dosages and sensitivity studies[8] of various strains of C. diphtheriae suggested that greater blood concentration of penicillin, 1 to 2 u./ml., might be necessary. Gerber et al.[9] have shown that 30,000 u. of penicillin injected intramuscularly every three hours yields a concentration of 1 to 2 u./ml. This amount was therefore adopted for the present study for children as well as for adults. In November, 1947 an opportunity presented itself to test the therapy suggested.

CASE REPORT

A 7 year old Puerto Rican girl was admitted to the hospital because of severe toxic faucial diphtheria. She was one of 17 members of two related families who lived together under crowded conditions in the most intimate contact. She had been ill five days with a sore throat, fever, malaise and a markedly swollen neck, and was being treated as a case of acute follicular tonsillitis with salicylates and sulfadiazine. On admission to the hospital on the 6th day of her illness the child was extremely toxic. The temperature was 38.2° C. and the pulse 118/min. and regular. She had a "bull neck" with large swollen lymph nodes and with edema extending down to the clavicles. The odor of the breath was fetid. A heavy, adherent, tenacious grayish white membrane covered

From the Willard Parker Hospital, New York, N.Y.
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both tonsils, the pillars, the uvula and the soft palate. Pulse was regular at 112 to 114/min. Heart sounds were of fair quality; blood pressure was 90/44 mm. Hg. The electrocardiogram showed evidence of toxic myocarditis. The liver was enlarged, the lower edge being felt 5 cm. below the costal margin. Nose and throat cultures were positive for a virulent strain of C. diphtheriae of the mitis type.

On admission the child was given large doses of diphtheria antitoxin, 35,000 u. intramuscularly and 40,000 u. intravenously. Penicillin was started intramuscularly in dosage of 50,000 u. injected every three hours; 20 ml. of 50% glucose solution was injected intravenously every 6 hours. Three days later, when the clinical condition appeared to be improving, the child suddenly died. Autopsy revealed: 1. pharyngeal diphtheria, 2. toxic degeneration of the myocardium and diphtherial myocarditis, 3. passive congestion and edema of lungs, 4. toxic degeneration of liver and kidneys, 5. toxic splenitis, 6. follicular necrosis of paravertebral and mastoid lymph nodes; perilymphadenitis, 7. congestion of adrenals, and 8. toxic encephalopathy.

Procedure and Results

Nose and throat cultures of all the remaining 16 members of the family showed that 10 individuals harbored C. diphtheriae. Six members of the family, five, ranging from 21 to 38 years, and one, aged 2 months, showed negative nose and throat cultures and negative Schick tests. They remained at home. One of the 10, an 18 year old male, who showed evidence of acute faucial diphtheria, was hospitalized and immediately treated with antitoxin and penicillin. He made an uneventful recovery. The nose and throat cultures became negative within 24 hours and remained negative until his discharge from the hospital. The other 9 members, ranging in age from 2 to 17 years, who had positive nose and throat cultures were admitted to a special ward. Alternate cubicles were left empty to separate one patient from the other. All 9 were Schick tested. Eight were Schick negative and one Schick positive. The latter, a child of three years, was promptly treated with penicillin. The other eight were observed without treatment for 4 to 5 days. Nose and throat cultures were made daily. The C. diphtheriae recovered were tested for virulence, type and penicillin sensitivity before penicillin treatment was begun.

The direct smears which were made at home and in the hospital were inoculated on Loeffler's serum agar and incubated for 24 hours. The Loeffler cultures were than streaked onto tellurite chocolate agar and blood agar plates and these organisms were later transplanted to the sugar media for further differentiation. It was found that all of the 11 patients hospitalized harbored C. diphtheriae of the mitis type.

Virulence of the C. diphtheriae was determined on guinea pigs. The ventral aspects of the animal was shaved and a suspension of the pure diphtheria culture was injected subcutaneously. After 3 to 5 days those areas that resulted in necrosis were read as positive, the others as negative. Eight of the 11 organisms were virulent and 3 nonvirulent.

Penicillin sensitivity tests were done with the pure C. diphtheriae cultures and various sensitivities were observed as recorded in Chart I.

Each patient treated received 30,000 u. of penicillin every 3 hours intramuscularly and nose drops of 1 ml. penicillin in solution (1,000 u./ml.) into each nostril every 2 hours during the waking day, until 5 consecutive daily cultures were negative.

A carrier was considered cleared of C. diphtheriae if, following the cessation of penicillin therapy, 5 consecutive daily cultures obtained from the nose and throat were negative for C. diphtheriae.

On the 10th hospital day the nose and throat cultures were still positive for C. diphtheriae in all of the eight untreated carriers. Four of these cases (Group A), beginning with the youngest and including an alternating older patient, were selected for penicillin treatment. The other four (Group B) were left untreated. Within 36 hours after penicillin treatment was started, the nose and throat cultures of the four patients in Group A were negative and remained negative for 5 consecutive days when treatment was discontinued and for the next 5 to 23 days, during which period they were observed.

On the 21st hospital day the 4 untreated cases still had positive nose and throat culture for C. diphtheriae. Two of these (Group B) were therefore treated with penicillin in the manner mentioned for Group A. These 2 also became negative within 36 hours. On the 25th hospital day 1 of the 2 remaining untreated cases (Group C) was also subjected to the penicillin therapy and her positive

CHART I

LABORATORY DATA

Case	Age and sex	Type of C. diph.	Penicillin sensitivity of C. diph. in u/ml.	Toxicity of C. diph.	Group	Result of culture of nose and throat
1	7 yr. F	Mitis	⊥ to 0.5	⊥	Diph.	Lung culture pos. at post mortem
2	18 yr. M	"	⊥ to 0.5	⊥	Diph.	Nose and throat neg. after 36 hrs. pen.
3	3 yr. M	"		⊥		Neg. after 5 days of pen.
4	2 yr. F	"	⊥ to 1.0	⊥	A	Neg. after 36 hrs. of pen.
5	5½ yr. M	"	− to 1.0	⊥	A	"
6	10 yr. F	"	⊥ to 1.0	−	A	"
7	12 yr. F	"	− to 1.0	⊥	A	"
8	10 yr. F	"	⊥ to .05	⊥	B	Pos. 21 days. Neg. after 36 hrs. pen.
9	17 yr. F	"	⊥ to 1.0	−	B	"
10	9 yr. F	"	⊥ to 0.5	⊥	C	Neg. 4 wks. Untreated.
11	4 yr. F	"	− to 1.0	−	C	Pos. 25 days. Neg. after 36 hrs. pen.

The column on "Penicillin sensitivity" indicates minimum penicillin concentration to which C. diphtheriae strain was (⊥) sensitive or maximum penicillin concentration to which particular strain was resistant (−).

Under "Results" are indicated nose and throat culture findings at various times after treatment with penicillin, unless otherwise stated.

A blank space indicates no determination made.

nose and throat cultures were promptly converted to negative. The last case was not treated because her throat culture had begun to be negative. She cleared up spontaneously in the 4th week.

COMMENT

All of the 11 patients hospitalized were found to harbor C. diphtheriae of the mitis type. Of these eight were virulent and three nonvirulent. Of the nine C. diphtheriae organisms tested for penicillin sensitivity, three were found resistant to one u. and six sensitive to one u./ml. of blood. Only two of the six were sensitive to 0.5 u./ml.

As has already been indicated, of the 11 patients admitted to the hospital, the first one, the seven year old child, died. C. diphtheriae was cultured from the lungs post mortem. The 18 year old with faucial diphtheria responded rapidly to treatment with antitoxin and penicillin in the dosage and via the route indicated. His nose and throat cultures became negative in 24 hours and remained negative thereafter. The three year old child with positive Schick test required five days of penicillin therapy before the nose and throat cultures became and remained negative. Seven of the remaining eight patients were cleared of their carrier state within 36 hours after penicillin therapy was instituted.

Thus it may be assumed that for this particular group of carriers penicillin as administered intramuscularly and by nose drops was rapidly successful in eight of nine and in one case of faucial diphtheria. This was also true for those harboring organisms resistant to penicillin 1.0 u./ml. in vitro. Whether penicillin levels in excess of 1.0 u./ml. were attained is not certain, since penicillin levels were not determined regularly. The studies of Baehr and Gerber would suggest that such levels were attained. Whatever they were they seemed adequate in these patients.

It is of course impossible to state which penicillin, that injected intramuscularly or that applied locally, was effective or whether both together affected a more rapid cure than might have either alone. The question studied was whether the dosages and routes of administration of penicillin would effect rapid clearing of the carrier state. The answer can be given in the affirmative. Previous experience[1] indicated that penicillin given by the intramuscular route was the more important since results were better than with penicillin sprayed on the nose and throat or dropped in the nose.

Further experience with penicillin administered as nose drops to diphtheria carriers is about to be reported by Troy.[10] His data indicate that there was some shortening of the period of the carrier state as compared to the controls, but that the results were not attained as rapidly nor as uniformly as in the group discussed in this report or those results previously observed with parenteral penicillin alone. Whether penicillin solutions of higher concentrations than 1,000 u./ml., e.g., 10,000 u./ml., as suggested by Levy,[7] are more uniformly effective when used as nose drops must stand further trial.

The usual health department regulations permit the discharge of a diphtheria carrier from hospital confinement after three consecutive daily negative cultures are obtained. The patients considered in this report actually had 10 consecutive daily negative cultures before discharge. The criteria for cure of the carriers were severe and believed adequate to establish a cure.

At present the efficacy of large daily doses of procaine penicillin is being investigated in the hope that the results will permit the discard of the disturbing procedure of multiple daily injections.

The combined use of penicillin 30,000 units injected intramuscularly every three hours and penicillin 1,000 u./ml. of physiologic saline solution administered in the form of nose drops every two hours during the day effected a cure in eight diphtheria carriers within 36 hours and in a ninth in five days, and in one case of faucial diphtheria. The diphtheria was of the mitis type in all. All organisms were resistant to a penicillin concentration less than 0.5 u./ml. and many to 1.0 u./ml.

Treatment was continued until five daily consecutive cultures were negative. After treatment five consecutive negative daily cultures were considered an indication of cure.

It is believed that the parenteral therapy was important in the results. A single large

dose of procaine penicillin is now being tried to attempt to obviate the multiple injection technic.

Conclusions

Penicillin administered intramuscularly in doses of 30,000 u. every three hours and concurrently in the form of nose drops 1,000 u./ml. in each nostril every two hours effectively eliminated C. diphtheriae from seven carriers and one case of faucial diphtheria within 36 hours. One carrier required five days of therapy.

Penicillin is an effective agent in shortening the period of the carrier state of chronic diphtheria carriers.

Addendum

Since the paper was submitted for publication six other cases of faucial diphtheria and a diphtheria carrier have been treated with single daily intramuscular injections of 300,000 u. of procaine penicillin in oil containing 2% aluminum monostearate.

Case Reports

1. A. McG., aged 4 yrs., was admitted on the 4th day of diphtheria of tonsils and pharynx. She received 25,000 u. of antitoxin intramuscularly and 15,000 u. intravenously and 300,000 u. of procaine penicillin in oil. Throat culture was positive for a toxic strain of C. diphtheriae. Culture became negative after 24 hours and remained negative for the next 5 weeks. Cultures were taken daily for the first 2 weeks and every 2 or 3 days thereafter. Penicillin was continued for 4 days.

2. M. DeC., aged 8 yrs., was admitted with laryngeal and tonsillar diphtheria. Throat culture was positive for a toxic strain of C. diphtheria. She received 20,000 u. of antitoxin intramuscularly on admission and the same amount the next day. Culture was negative after 24 hours and remained so for the 4 week period of hospitalization. Penicillin was continued for 4 days.

3. V. R., aged 2 yrs., was admitted with tonsillar diphtheria. She had been treated with sulfadiazine and 2 days prior to admission had received an injection of 150,000 u. of procaine penicillin in oil. Nose and throat cultures were positive for toxic strains of C. diphtheriae. 15,000 u. of antitoxin were injected intramuscularly and 15,000 u. intravenously on admission. Nose and throat cultures were positive on admission and on the next day. Thereafter they were negative daily for 2 weeks and every 2nd or 3rd day for the next 2 weeks, after which she was discharged. Penicillin was continued for a total of 6 days, or 4 days after cultures became negative.

4. A sister of V. R., aged 6 yrs., was admitted with tonsillar and pharyngeal diphtheria. Nose and throat cultures were positive for toxic C. diphtheriae. She received 20,000 u. of antitoxin intramuscularly. Cultures became negative on the 3rd day and except for 1 casual positive culture 5 days later remained negative for the 4 week period of observation. Penicillin was given for the first 7 days and for another 5 days after the isolated positive culture. The culture taken on the 9th day after admission was negative and in all probability the second series of penicillin injections were unnecessary.

5. M. C., aged 3 yrs., with tonsillar diphtheria was admitted on the 3rd day of her disease. Her culture was positive for C. diphtheriae. Penicillin was started on admission and continued for 7 days. Because of a prolonged conduction time of .20 sec. shown by ECG, she was observed for a 5 week period throughout which nose and throat cultures were negative.

6. M. B., aged 5 yrs., was admitted on the 4th day of illness. She was given 15,000 u. of antitoxin intravenously and 15,000 u. intramuscularly. Nose culture was positive for C. diphtheriae on admission and throat culture was positive 1 day later. Penicillin was administered for 6 days. Nose and throat cultures were negative after the 2nd day and have remained so.

7. E. S., aged 6 yrs., was admitted as an incidental carrier. Throat cultures were positive for C. diphtheriae on admission but became negative after 2 days of treatment and remained so until discharge.

8. R. H., aged 7 yrs., was admitted as a diphtheria carrier. His Schick test was negative. Nose and throat cultures were positive for nontoxic strains of C. diphtheriae. Penicillin was given for

9 days. Throat cultures were positive for 3 days, then negative for 3 days, then became positive again. The patient was discharged because the organism was nontoxic.

These data indicate that penicillin is effective when administered in single daily doses for eradication of C. diphtheriae from the nose and throat. These and previous findings indicate that all cases of diphtheria should be treated with antitoxin and penicillin preferably in large single doses of procaine penicillin in oil. It is conceivable that larger doses will be necessary for older children and adults, and possibly for more resistant strains of bacteria.

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Spanish Abstract

Tratamiento de Portadores de Difteria con Penicilina

El uso combinado de 30,000 unidades de penicilina inyectadas intramuscularmente cada tres horas y de 1,000 U./ml penicilina de solución salina fisiológica administrada en forma de gotas para la nariz cada horas durante el día afectaron una cura en ocho portadores de difteria dentro de 36 horas y en un noveno en cinco días, y también en un caso de difteria faucial. En todos la difteria era de tipo mitis. Todos los organismos estaban resistentes a la concentración de penicillin menos de 0.5 u. y muchos a la de 1.0 u./ml.

El tratamiento fué continuo hasta que se tuvieron cinco cultivos consecutivos diarios que resultaron negativos. Se cree que la terapia parénterica fué importante en los resultados. Se está tratando una sola dosis de penicilina procaina para ver si se puede evitar la técnica de inyección múltiple.

888 Park Avenue

INTESTINAL ABSORPTION OF VITAMIN A FROM OILY AND AQUEOUS MEDIA IN PATIENTS WITH THE CELIAC SYNDROME

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THIS article presents a series of observations on the absorption of vitamin A from aqueous and oily media by patients with the celiac syndrome. Clifford and Weller[1-2] have shown that higher blood levels of vitamin A are obtained in prematurely born infants when aqueous preparations are administered than when oily concentrates are given. This observation has been confirmed by Lewis et al.[3] in full term infants, older children and adults, and they obtained a normal vitamin A absorption curve in one child with cystic fibrosis of the pancreas when an aqueous preparation of vitamin A alcohol was administered. Kramer et al.[4] have demonstrated that vitamin A is more readily absorbed from aqueous dispersions than from oily preparations. Their report includes observations on five normal infants and children and five patients with celiac disease.

The purpose of this study, begun shortly after Clifford's earlier report,[1] was (a) to compare the absorption of vitamin A acetate and vitamin A alcohol in patients with cystic fibrosis of the pancreas, and (b) to compare the absorption of vitamin A from aqueous and oily media in patients with cystic fibrosis of the pancreas and idiopathic celiac disease.

METHODS

Patients were selected for this study at the time of admission to the hospital. A duodenal drainage was performed on each child according to the technic of Andersen,[5] but omitting the preliminary period of hydration. The absence of trypsin or an extremely low level of this enzyme was usually confirmed by a second drainage before a diagnosis of cystic fibrosis of the pancreas was made. All of the children with idiopathic celiac disease had clinical evidence of the disease to support the laboratory findings.

The vitamin A absorption curves were performed as outlined by Breese and McCoord,[6] and modified by May et. al.[7] except that a Colman Universal Model 11 spectrophotometer was used in place of the Evelyn photoelectric colorimeter. Blood samples were drawn before giving the vitamin A, and at 3, 5 and 8 hour intervals. In all instances, vitamin A concentrates were omitted from the diet for the 24 hour period immediately preceding the test. After the ingestion of the calculated dose, the usual dietary regimen was followed, omitting prescribed preparations containing vitamin A.

The dose of vitamin A given to each child in each experiment was 5,000 U.S.P. units/kg. body weight. The preparations* used were: (a) oleum percomorphum with 65,000 U.S.P. u. vitamin A/gm.; (b) vitamin A alcohol dissolved in 70% propylene glycol with 52,600 U.S.P. u./ml.; (c) vitamin A acetate dispersed on dextri-maltose with 55,400 U.S.P. u./gm.; (d) vitamin A alcohol

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dispersed on dextri-maltose with 50,800 U.S.P. u./gm.; (c) oleum percomorphum dispersed on dextri-maltose with 3,085 U.S.P. u. vitamin A/gm.; (f) a special water-paste emulsion of vitamin A alcohol containing 58,450 U.S.P. u./gm.

Results

The absorptions curves obtained after administering the various vitamin A preparations to 6 patients with cystic fibrosis of the pancreas are shown in Figure 1. In all instances, the curves were completely flat when the vitamin was given in percomorph oil and almost as flat when given as an aqueous suspension of percomorph oil dispersed on dextri-maltose. In the three instances where comparisons can be made (R. G., S. E., and J. J. M.), there is some evidence of enhanced absorption from the dispersed product, but the improvement is so slight that its importance is questionable.

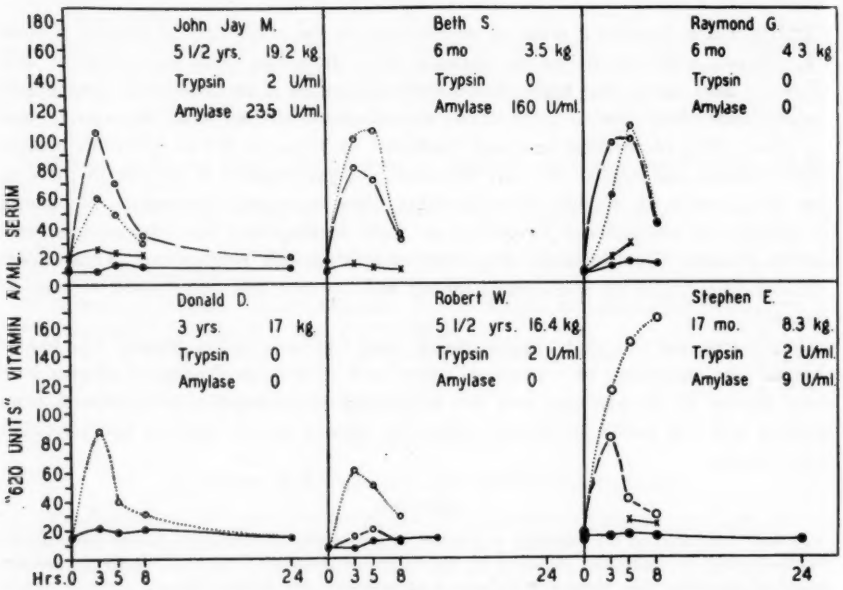

Fig. 1. Vitamin A absorption curves in children with cystic fibrosis of pancreas. (5,000 U.S.P. Units vitamin A/kg. body weight.) ——●—— percomorph oil; ——✕—— percomorph oil dispersed on dextri-maltose; ·····⊙····· vitamin A acetate dispersed on dextri-maltose; — —⊙— — vitamin A alcohol dispersed on dextri-maltose.

However, when an aqueous suspension of either vitamin A acetate or vitamin A alcohol dispersed on dextri-maltose was given to these same children, the serum levels indicated excellent absorption.

The absorption curves obtained after administering oily and aqueous preparations of vitamin A to four patients with idiopathic celiac diseases are shown in Figure 2. It is to be noted that the administration of vitamin A in percomorph oil results in absorption curves which are just as flat as in the previous group of children with cystic fibrosis of the pancreas. This flat response to an oily preparation has been observed in more than half of the patients studied with idiopathic celiac disease. When an aqueous suspension of vitamin A alcohol dispersed on dextri-maltose was given to these same children, there was only a slight rise in the absorption curves. The average response in the four instances was only 14 "620 units." None of the curves rose into the normal range, which is in striking contrast to the marked elevation observed in the cystic fibrosis group.

Data obtained from three additional children with idiopathic celiac disease are shown in Figure 3. A glance at the curves will reveal that the results are of the same magnitude as those shown in Figure 2. One of these patients (R. G.) was given a special water-paste emulsion of vitamin A alcohol.

The other two were given vitamin A alcohol dissolved in 70% propylene glycol. Observations were made on one of these children (P. H.) after 8 months of therapy which included crude liver extract, vitamin B complex and folic acid. Vitamin A acetate dispersed on dextri-maltose was used following this period of treatment.

Discussion

The results which are presented in this report demonstrate that vitamin A acetate and vitamin A alcohol can be absorbed from an aqueous dispersion by patients with cystic fibrosis of the pancreas. A comparison may be made between the response to the two

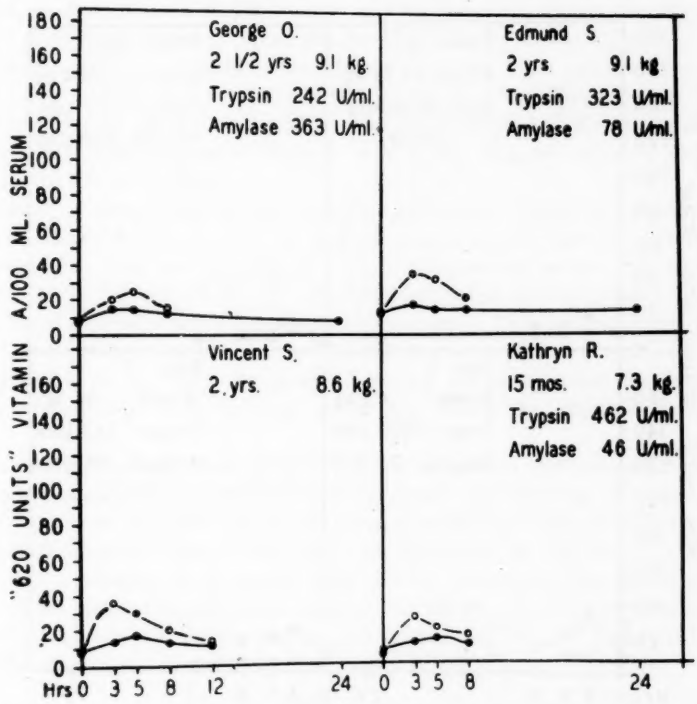

FIG. 2. Vitamin A absorption curves in children with idiopathic celiac disease. (5000 U.S.P. Units vitamin A/kg. body weight.) ——●—— percomorph oil; — — ⊙ — — vitamin A alcohol dispersed on dextri-maltose.

forms in four of the patients (J. J. M., B. S., R. G. and S. E.). Both forms of the vitamin were dispersed on the same vehicle (dextri-maltose) and were present in the preparations in about the same concentration. In these cases, the mean rise of the serum vitamin A level above the percomorph oil curves was 95 "620 units" for the acetate, and 77 for the alcohol. The acetate curves rose above the alcohol in three of the four instances.

Comparatively poor results were obtained in one patient (R. W.) with both the vitamin A acetate and alcohol. They have been excluded in computing the above mean values. This boy was studied for four years. He has extensive bronchiectasis, emphysema, chronic cyanosis, and marked clubbing of the fingers and toes. At the time the vitamin A absorption tests were performed, he was recovering from pneumonia attended by

myocardial failure. The severity of the infection and the cardiac decompensation may account, at least in part, for the poor absorption.

The results of this study are similar to those reported by May and Lowe,[8] but differ in some respects from the observations of Clausen et al.[9, 10] May and Lowe have obtained a mean rise in the vitamin A absorption curves of 119 "620 units" when an emulsion of vitamin A acetate (15% vitamin A acetate, 15% Tween 20, and 70% water) was given to 11 patients with cystic fibrosis of the pancreas, and a mean rise of 104 "620 units" when crystalline vitamin A alcohol (3,000 I.U./gm.) was mixed with applesauce and

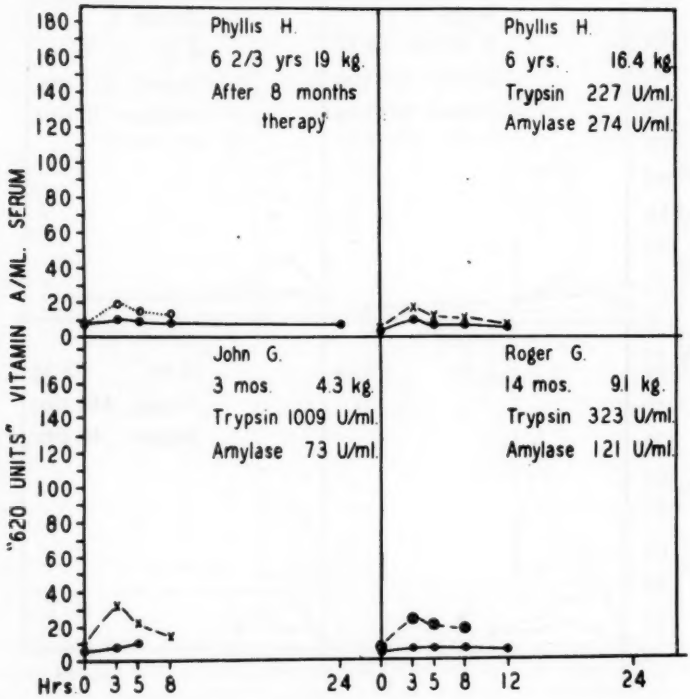

FIG. 3. Vitamin A absorption curves in children with idiopathic celiac disease. (5000 U.S.P. Units vitamin A/kg. body weight.) ——●—— percomorph oil; ·····⊙····· vitamin A acetate dispersed on dextri-maltose; — —×— — vitamin A alcohol in 70% propylene glycol; ——⊗—— special water-paste emulsion of vitamin A alcohol.

given to two patients. Although these observations are similar to ours, they are not entirely comparable since the two forms of the vitamin were administered in different preparations. In definite contrast are the findings of Clausen and co-workers. Their studies[10] now include observations on 13 patients with cystic fibrosis of the pancreas who absorbed the alcohol form of vitamin A much better than the ester. Both forms of the vitamin were given by mouth as oily concentrates which contained 210,000 I.U./gm. Whether this difference in results is due to the oil or to variations in the absorbability of the simple acetate and the naturally occurring esters (probably high molecular weight fatty acid esters) remains to be determined. May and Lowe[8] and Kramer and co-workers[4]

have demonstrated that emulsification enhances the absorption of vitamin A. It has also been shown[8] that the absorption of the naturally occurring esters by patients with cystic fibrosis of the pancreas can be markedly improved provided the oil droplets in the emulsion are sufficiently minute. However, the number of cases studied is small. Additional observations are needed to definitely establish whether there is constantly a difference in the absorbability of vitamin A alcohol, vitamin A acetate and the naturally occurring esters of vitamin A.

The fact that vitamin A was absorbed only slightly better from percomorph oil dispersed on dextri-maltose than from the oil itself seems to indicate that the dextri-maltose has no significant effect on the absorbability of the vitamin as it occurs in the oil.

The results of this study indicate that vitamin A alcohol in an aqueous dispersion is absorbed only slightly better by patients with idiopathic celiac disease than is vitamin A from percomorph oil. This is in accord with data published by Kramer et al.,[4] and lends supports to the suggestion made by May et al.[11] that the defect in absorption lies within the intestinal mucosa.

A number of factors affecting the absorption of vitamin A from the intestinal tract have been clarified by the work of Lewis et al.[3] who have used some of the vitamin A preparations that have been investigated here. In observations on seven normal infants they were able to demonstrate that less vitamin A is excreted in the feces when it is given in an aqueous dispersion rather than in an oily concentrate. They confirmed this observation in a series of animal experiments and added data which indicated that more vitamin A was stored in the liver after the aqueous dispersion was administered. They concluded that the superior response is due to the greater dispersion of the vitamin in the aqueous vehicle.

Lewis and collaborators[3] have pointed out that the studies with aqueous dispersions of vitamin A make it necessary to re-evaluate the vitamin A requirement of normal infants and children. From the difference in the response to oily and aqueous preparations by patients with idiopathic celiac disease and cystic fibrosis of the pancreas, it is apparent that an oily preparation of the natural esters must be used as a diagnostic test in cystic fibrosis of the pancreas. It also seems apparent that the absorption curves plotted for an aqueous and an oily preparation may be used by the clinician as a further aid in the differential diagnosis of these two types of intestinal insufficiency.

Summary

The absorption of vitamin A from oily and aqueous media has been studied in infants and children with cystic fibrosis of the pancreas and idiopathic celiac disease.

Patients with cystic fibrosis of the pancreas can absorb vitamin A acetate and vitamin A alcohol when it is given to them in an aqueous dispersion. The vitamin A acetate curves rose above the vitamin A alcohol curves in three of four patients on whom absorption curves were obtained.

Vitamin A is absorbed by patients with idiopathic celiac disease only slightly better from an aqueous dispersion of the alcohol than from an oily concentrate of the naturally occurring esters. The poor absorption from an aqueous media by these patients supports the suggestion that the defect in absorption in this disease lies within the intestinal mucosa.

The use of the differences in response to oily and aqueous concentrates in the differential diagnosis of the entities of the celiac syndrome is suggested.

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SPANISH ABSTRACT

Absorción Intestinal de Vitamina A de Media Aceitosos y Acuosos en Pacientes con Síndrome Celíaco

Se ha estudiado la absorción de vitamina A de media aceitosos y acuosos en seis infantes y niños con fibrosis cística del pancreas y en siete pacientes con enfermedad celíaca idiopática.

Pacientes con fibrosis cística del pancreas pueden absorber acetato de vitamina A y alcohol de vitamina A cuando se les da en una dispersión acuosa. Las curvas del acetato de Vitamina A subieron más que las curvas del alcohol de vitamina A en tres de los cuatro pacientes en quienes se obtuvieron ambas curvas de absorción. El alza principal de la cantidad de vitamina A de suero arriba de las curvas de aceite fué 95 "629 unidades" para el acetato, y 77 para el alcohol.

La vitamina A es absorbida por pacientes con enfermedad celíaca idiopática solamente un poco mejor de una dispersión acuosa del alcohol que de un concentrado aceitoso de ésteres que ocurren naturalmente. La mala absorción de media acuosos por estos pacientes respalda la sugerencia de que el defecto en la absorción en esta enfermedad está dentro de la mucosa intestinal.

Se sugiere el uso de las diferencias en respuesta a los concentrados acietosos y acuosos en la diagnosis diferencial de las entidades del síndrome celíaco.

19th Avenue at Downing

HOMOLOGOUS SERUM HEPATITIS IN INFANTS AND CHILDREN

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DURING the past two years eight cases of hepatitis in infants who had been transfused with blood or plasma or with both have been observed. Five of these infants died with acute hepatic degeneration. The literature reveals that infectious hepatitis, serum jaundice and acute hepatic atrophy are all relatively uncommon in infancy.

Although it had been well recognized that hepatitis at times followed the administration of human blood, serum or plasma, the numerous investigations during the recent war years have brought about an increase in knowledge concerning the etiology and clinical aspects of this disease. The extensive use of blood and plasma in the military forces resulted in an incidence of homologous serum jaundice that made this condition a major problem.[1-3] In addition, it has been estimated[4] that, in 1942, 23,000 cases of hepatitis followed the administration of yellow fever vaccine which contained icterogenic human serum. The ready availability of blood and pooled plasma from hospital or community blood banks, through commercial sources, or through the distribution of surplus dried plasma by the American Red Cross, has resulted in an increased use of these materials.

There have been several recent papers from civilian hospitals and a public health source [5-8] reporting the occurrence of homologous serum jaundice in the recipients of blood and plasma.

In contrast to the voluminous literature on this disease in adults, little has been written on the occurrence of homologous serum hepatitis in children. Most authors[9] stress the increased resistance of children below the age of five years to both infectious hepatitis and serum hepatitis. Scheinberg et al.[5] report that, with the exception of one questionable instance, no cases have been recognized at the Children's Hospital in Boston where a considerable amount of pooled plasma has been used. The incidence of jaundice in their entire series including adults was one case in every 86 plasma transfusions. In a follow-up study of 649 recipients of one or more transfusions of Red Cross surplus dried plasma, Brightman and Korns[6] reported an incidence of 30 cases (4.6%) of homologous serum hepatitis. However, there were no cases in 78 recipients under 19 years of age. The latter authors also surveyed a series of 51 fatal cases of hepatitis reported to the New York State Board of Health and ascribed 15 of these to probable serum hepatitis. One of the deaths occurred in a five year old child but the details of the illness are not given. Spurling,[10] in a follow-up study of 1,054 recipients of pooled plasma or serum, found an incidence of 7.3% of serum hepatitis. He commented upon the increased incidence in the older age groups and found no case under four years of age. Oliphant[11] also noted an increased resistance to hepatitis among

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individuals under 20 years of age who received icterogenic yellow fever vaccine in the Virgin Islands.

The British experience[12] with several lots of icterogenic measles convalescent serum is not in keeping with the above reports that indicate increased resistance to serum hepatitis in children. In 1937, 41 of 109 recipients of a single lot of measles convalescent serum developed jaundice and there were eight deaths in this group. In another group of 158 recipients of measles convalescent serum, there were 23 cases of jaundice with one death. The report did not analyze the cases in relation to the age of the recipients but it was stated that the recipients were mostly young children and those attending schools. Only four deaths are reported in any detail and these were in children 13 years, 10 years, 7 years and 10 months, respectively. In the United States, Bruyn[13] has reported recently a fatal case of homologous serum jaundice in a 3½ month old infant who had received transfusions in the neonatal period for possible erythroblastosis. Sidbury and Hall[14] have also reported a single case of serum hepatitis with recovery in a three year old child who had received pooled plasma three months previously.

Early reports on the incidence of acute yellow atrophy of the liver in infants and children are somewhat confusing because of the multitude of implicated etiologic factors. Amberg[15] states that acute yellow atrophy is rare during the first year of life. Up to 1929 Rolleston and McNee[16] collected 42 cases in which the patients were under 10 years of age. To this total, Amberg added 14 cases, but the role of virus hepatitis and serum transmitted virus in particular was not studied. Wallgren[17] described three cases of acute hepatic necrosis in infants aged 2½ months, 2 years and 3 years which occurred during an epidemic of "catarrhal icterus." Two similar cases, aged 21 months and 7 years, were added by Amberg. In 1926, Karelitz[18] autopsied a 13 month old child who died of acute hepatic necrosis and whose twin brother was ill with "catarrhal jaundice" at the time.

Clinical Material

Table I reveals that the four deaths in the cases seen in 1947 occurred within a three week period. The first case was in a 2½ year old Puerto Rican girl who became ill with fever and an enlarged liver 31 days after she received a plasma transfusion during treatment for a burn. She developed jaundice and died within a few days. The second patient was admitted with severe diarrhea and received plasma transfusions 36 to 40 days before the onset of jaundice in the course of treatment for acute severe diarrhea. The third patient had also received plasma and blood between 47 and 53 days before the onset of jaundice. The fourth patient was admitted originally with erythroblastosis fetalis for which a replacement transfusion was performed. Forty days later, she was readmitted because of anemia, vomiting and fever. Jaundice developed and the patient died in cholemia five days after admission.

The first three patients had received reconstituted dried plasma distributed from military surplus stocks. Unfortunately, no record was kept of the lot numbers of the plasma used and therefore it is not known whether a single icterogenic lot was implicated. Since all the transfusions had been given within a two week period, this seems to be a likely possibility, especially since a single unit of plasma had been shared frequently among several infants. Case 4 had received blood from a professional donor who was traced and found to be in good health two months after the date of the transfusion. He had no symptoms suggestive of hepatitis and he had served as a donor both before and after

the transfusion given to the patient without any complications. The replacement transfusion was done on the same day and in the same treatment room used for the plasma transfusion in Case 2. It is therefore possible that transmission of the virus may have occurred through the use of contaminated equipment. All syringes and needles used for the transfusion had been autoclaved. The needles used for the withdrawal of blood had also been autoclaved. The syringes used for the withdrawal of blood for chemical analyses had not been invariably autoclaved.

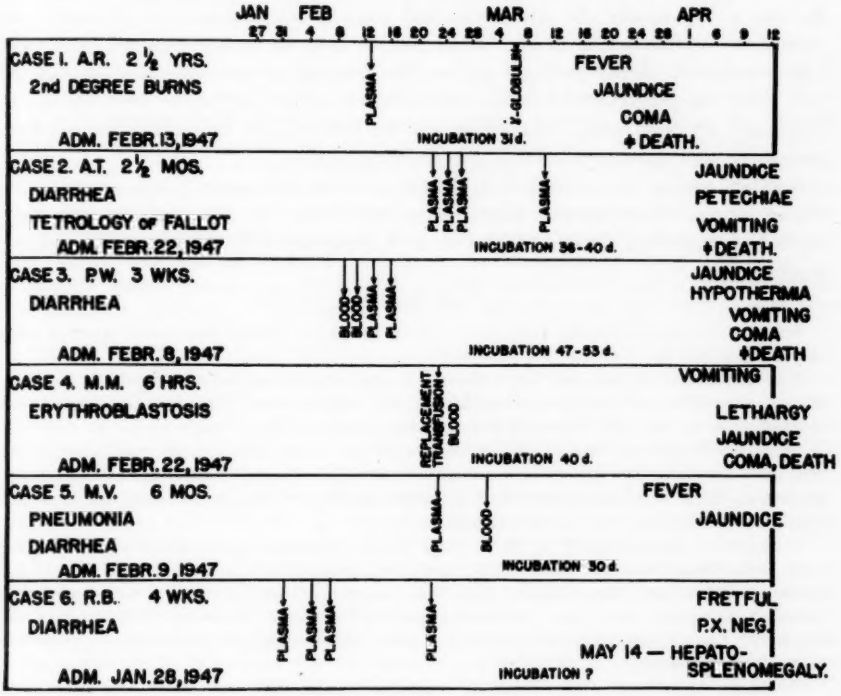

TABLE I

INDICATES RELATIONSHIP OF TRANSFUSIONS OF PLASMA AND BLOOD TO ONSET OF HEPATITIS AND OUTCOME OF DISEASE IN SIX PATIENTS ADMITTED TO MT. SINAI HOSPITAL WITHIN PERIOD OF JANUARY 28, 1947 TO FEBRUARY 22, 1947.

Since all these four patients with hepatitis had received blood or plasma transfusions between January 31 and February 28, an attempt was made to follow all other infants who had received plasma during this period. Of 20 such cases we were able to trace nine infants. Of these seven were well and physical examination revealed no abnormality. Cephalin flocculation tests done on these patients showed a 2 plus reaction in two instances; the others were negative. It was found that one infant had become febrile 30 days after he received plasma. He became jaundiced five days later and was admitted to another hospital with a diagnosis of acute hepatitis. He is reported as Case 5 in this series. Another infant (Case 6), who had received four plasma transfusions between

Jan. 31 and Feb. 21 developed marked hepatosplenomegaly and is reported as a case of hepatitis without jaundice.

Other infants on the ward during the month of February who had not received plasma were seen in the follow-up clinic and there was no evidence of hepatitis in this group. There had been no cases of jaundice under treatment on the ward during February, nor were any suggestive symptoms of hepatitis elicited from thorough questioning of the ward personnel.

A seventh case of hepatitis had been seen in this hospital during the preceding year. He was a 5½ month old infant who had received two transfusions for anemia of prematurity at four weeks of age. Three months later he became jaundiced and there was enlargement of the liver and spleen. The jaundice persisted for seven weeks and then there was progressive cholemia with shrinkage of the size of the liver, and death. Permission for postmortem examination was not obtained but the clinical findings were compatible with serum hepatitis and acute liver degeneration.

Another patient was admitted in February 1948 with anemia and periostitis of obscure origin. Three months after a blood transfusion he developed hepatitis from which he is recovering slowly. At this time he is apparently well but there is still moderate hepatomegaly.

Case Reports

Since the postmortem findings were of a uniform character, a detailed postmortem report is given only in Case 1.

Case 1. A. R., a 2½ year old Puerto Rican girl, was admitted to the hospital on Feb. 13, 1947, 45 min. after both lower extremities were burned with boiling water. There were 2nd degree burns over both legs and feet with edema, erythema and varying-sized bullae.

Emergency treatment consisted of debridement of the burned areas under ethyl chloride and drop ether anesthesia. The wounds were dressed with sterile vaseline gauze and compression bandages. Intravenous fluids were administered by continuous infusion for the first 36 hours and 200 cc. of pooled Red Cross plasma were given intravenously.

Temperature ranged from 38° to 39.5° C. for the first 72 hours but subsided thereafter to a low grade level. Penicillin, 30,000 units every 3 hours, was given intramuscularly between Feb. 13 and March 17. The burned areas remained clean. She was afebrile after 2 weeks and after 4 weeks the wounds were healed except for a granulating area on the dorsum of the right leg and heel. On March 7, 2.7 cc. of immune serum globulin was given intramuscularly as prophylaxis after exposure to measles on the ward.

On March 15, 31 days after admission, temperature rose suddenly to 39.5° C. but she did not appear acutely ill. Physical examination revealed only enlarged tonsils and small cervical lymph nodes. The temperature rose to 39.8° C. on March 16 and to 40.4° C. on the following day.

On March 19 she became restless and irritable. She cried a great deal, tossed about in bed, and her sensorium was clouded. Her sclerae were jaundiced. Liver was enlarged to 4 cm. below the costal margin and the tip of the spleen was just felt. Her urine contained bile, and urobilinogen was present to a dilution of 1:5. The blood icterus index was 30 (acetone method) and the total protein 5.3 gm./100 cc. blood.

The temperature remained normal from March 19 to March 21 but her general condition deteriorated and her lethargy deepened. She was treated with a continuous intravenous infusion of dextrose 5% in normal saline alternating with dextrose 10% in distilled water.

On March 21 she became comatose and reacted only to painful stimuli. Jaundice of the skin and sclerae became more intense. Respirations were deep and rapid. Lungs were clear. Heart sounds were rapid and forceful. Abdomen was somewhat distended and a soft splenic edge was palpable 3 cm. below the costal margin. Liver edge had receded from 4 cm. to 1 cm. below the costal margin. There was generalized hypotonicity but the deep tendon reflexes were moderately hyperactive. There were no meningeal signs. On March 22, the temperature rose to 40.4° C. and she remained comatose. Her respirations were stertorous and there was cyanosis of the skin and mucous membranes. There

was bleeding from the nose. Coarse moist rales were heard throughout the chest. The liver edge was no longer palpable. She was placed in an oxygen tent and given a transfusion of 100 cc. of blood. The cyanosis became more intense even in oxygen and the patient died on March 23.

Laboratory examinations performed during the terminal phase of the illness revealed the following: Hgb. 8.1 gm./100 cc. WBC count 24.1 thousand/cmm. with polymorphonuclear cells 50%, lymphocytes, 48% and monocytes, 2%. Urinalysis: trace of albumen; 4 to 6 pus cells/hpf; bile 3 plus; urobilinogen present in 1:5 dilution. Plasma CO_2 content was 23 volumes per cent, the total protein 6.6 gm./100 cc. blood, the icterus index 50 (acetone method), the urea N 10 mg./100 cc. blood, the cephalin flocculation 2 plus, and the blood sugar 25 mg./100 cc. blood and 10 mg./100 cc. Blood culture grew Staph. albus B in one flask and a Str. viridans in another.

Postmortem Findings:

Macroscopic Findings. Abdominal cavity contained 300 cc. of clear fluid. There were petechiae in the serosa and ecchymoses in the perirenal tissues. Pleural cavities contained about 250 cc. of slightly hemorrhagic fluid, and the pleural surfaces revealed petechiae. Liver edge was somewhat above the right costal margin. Liver was markedly reduced in size, weighing 195 gm. (normal weight 400 gm.), and its consistency was less firm than normal. Its surface showed some irregularities consisting of many tiny yellow nodules which were slightly raised and set off from the otherwise dusky red surface. On the cut surface, a fine red and yellow network pattern was noted. Bile was present in the gallbladder and large biliary ducts. Spleen was enlarged to about twice the normal size. Kidneys were pale and showed hemorrhages in the perirenal tissues. Lungs were heavy from edema and marked engorgement. Upper small intestine was edematous and showed hemorrhages in the mucosa. Lymphoid tissues were not prominent. Remaining organs revealed no noteworthy changes.

Microscopic Findings: Liver: There was an almost uniform massive destruction of the liver parenchyma due to autolytic necrosis of most of the liver cells. Scattered through the lobules were a few remaining dying liver cells with pyknotic nuclei and degenerating cytoplasm, and large numbers of macrophages as well as small mononuclear cells and only a few polymorphonuclear leukocytes. The degenerating liver cells and the macrophages contained sudanophilic material. The destruction of the liver cells was complete, and there was no evidence of regeneration. The framework of the liver was collapsed and the sinusoids engorged with blood. Many of the central veins showed a strongly eosinophilic staining reaction; occasionally there was a mild inflammatory reaction in the wall of a vein. At the periphery of the lobules there was considerable proliferation of bile duct epithelium. Biliary thrombi in small ducts were numerous. In contrast to the central part of the lobules there was a striking inflammatory infiltration with many polymophonuclear leukocytes in the peripheral portions.

The gallbladder and the wall of the stomach showed severe edema, and there was a mild inflammation of the mucosa of the duodenum. The spleen showed congestion and a moderate infiltration with inflammatory cells. The centers of the Malpighian follicles showed phagocytic activity. Similar reactive centers were seen in the lymph follicles in the intestinal tract. A periportal lymph node showed an acute lymphadenitis.

In the kidney there was extensive fatty infiltration of the tubular epithelium, which showed atrophy and flattening in places. There were multiple bile-stained casts and small calcific deposits within some of the tubules. The glomerular capsules frequently were distended with an amorphous eosinophilic material. The lungs showed edema and an acute focal bronchopneumonia. The brain was normal.

Final diagnosis: Acute diffuse necrosis of the liver. Ascites. Icterus. Subserous and submucous petechiae and pulmonary hemorrhages. Splenomegaly. Edema of the lungs and hydrothorax.

Case 2. A.T., a 2½ week old male infant, was admitted to the hospital on Feb. 22, 1947 with a history of diarrhea and weight loss of 10 days' duration, and cyanosis from birth. On admission, he was dehydrated and in shock. A loud systolic murmur was heard over the entire precordium. Abdomen was slightly distended and the liver edge was felt 4 cm. below the costal margin.

Plasma CO_2 content was 17 volumes per cent, total protein 4.9 gm./100 cc. blood and hematocrit 40%. Roentgenogram of the chest showed the apex of the heart to be elevated with no other change in the cardiac contour. Lungs were clear. ECG showed sinus tachycardia and right axis deviation.

The infant was placed in an oxygen cubicle and treated with a continuous intravenous infusion,

starting with M/6 sodium lactate and followed by dextrose 5% in half-strength physiologic saline. Transfusions of reconstituted Red Cross plasma were administered on Feb. 22 (60 cc.), Feb. 24 (60 cc.), Feb. 26 (70 cc.), and March 11 (60 cc.). The patient improved with this regime. Liver, which had been enlarged to 4 cm. below the costal margin on admission, had receded to 2 cm. below the costal margin before discharge on March 21.

The patient was readmitted to the hospital on April 4, 1947. He had remained well until the morning of admission at which time his mother noted that his skin had become yellow in color. Jaundice deepened perceptibly during the day and the infant refused his feedings. On examination he was severely ill and toxic in appearance. Skin was cyanotic and when blanched by pressure a jaundiced tinge was noted. There was a diffuse petechial eruption over the entire body. Lungs were clear. Heart was enlarged and a loud systolic murmur was heard over the 3rd and 4th intercostal spaces at the left sternal border. Liver was felt 6 cm. below the costal margin. Spleen was palpable 5 cm. below the costal margin.

Hgb. 17.8 gm./100 cc. blood and WBC count 20,000. Plasma CO_2 content was 31 volumes per cent, total protein 5.3 gm./100 cc. blood and hematocrit 68%. Cephalin flocculation was positive (3 plus).

Temperature on admission was 35° C. and he was placed in an oxygen incubator. Parenteral fluids were given by clysis. His condition deteriorated rapidly and his diapers were deeply bile-stained. Respirations were labored and slow. He vomited bloody mucus in small amounts. There were clonic movements of the arms and legs. He died 8 hours after admission.

Final diagnosis: Acute diffuse necrosis of the liver. Icterus. Petechiae of skin and serous membranes. Focal pulmonary hemorrhages. Congenital heart disease: Tetralogy of Fallot. Diffuse mucopurulent bronchitis. Congestion of viscera. Fatty changes of kidneys.

Case 3. P.W., a 22 day old male infant, was admitted to the hospital on Feb. 8, 1947 with severe diarrhea and progressive loss of weight for four days. He was dehydrated and critically ill. Respirations were 82/min. and temperature was 36° C. There was moderate abdominal distention. Hgb. 9.8 gm./100 cc. blood and hematocrit 37%. The plasma CO_2 content was 7.8 volumes per cent.

He was treated with a continuous intravenous infusion starting with M/6 sodium lactate 275 cc. and followed by Ringer's-lactate solution with dextrose 5%. Citrated blood transfusions of 70 cc. and 60 cc. were administered on Feb. 9, and reconstituted Red Cross plasma was transfused on Feb. 10 (70 cc.) and Feb. 14 (60 cc.). He improved rapidly and was discharged from the hospital on March 11. He had gained 500 gm. during the period of hospitalization.

The patient continued to do well and had gained 660 gm. during the next 3 weeks. On April 3, 43 days after his first transfusion, a yellowish discoloration of the skin and sclerae was noted. Urine was dark yellow and the stools were lighter than usual. He took his feedings well and did not appear ill. However his temperature was 35° C. and he was referred for hospitalization. He had been cared for in a foster home in which there was no contact with any individual with jaundice. On examination, the patient did not appear ill. Temperature was 36.5° C. There was a faint icteric tint to the skin and sclerae. Liver was palpable as a sharp edge 3 cm. below the costal margin and the spleen was felt 2 cm. below the costal margin.

Hgb. was 9.0 gm./100 cc. blood and WBC count 31,400 with polymorphonuclear cells 23%, lymphocytes 67% and atypical lymphocytes 4%, similar to those described in infectious mononucleosis. Urine was negative for albumen and sugar but contained a trace of bile. Blood urea N was 8 mg./100 cc., the blood sugar 60 mg./100 cc., the icterus index 42 (acetone method), the serum alkaline phosphatase 84 King-Armstrong units (normal 15). Heterophile agglutination was positive to a dilution of 1:8. Blood culture was sterile.

A high protein, high carbohydrate, low fat formula was prescribed. 1.5 gm. of choline was given daily. The clinical course was uneventful for the first 4 days of hospitalization. His temperature was normal. He took his feedings well and did not vomit. The jaundice deepened moderately and the stools were light in color. On April 7 his condition became worse. The jaundice was much more marked and the icterus index had risen to 63. He was lethargic, refused most of his feedings and vomited several times. He was dyspneic with rapid moist respiration. He was apathetic and assumed the position of opisthotonus. A nauseating, sweet odor was noted on the breath. Liver rapidly decreased in size and was just palpable at the costal margin. Heart rate was rapid with a gallop rhythm. Despite treatment with a continuous intravenous infusion of dextrose 10% solution, oxygen and stimulants, his course was rapidly downhill during the day. Terminally there were frequent

generalized convulsions and clonic twitching of the extremities which were not improved with the intravenous administration of calcium gluconate. The patient died on April 8, 1947.

Final diagnosis: Acute diffuse necrosis of the liver. Icterus. Enlargement of the spleen. Fatty changes of kidneys. Nodular bronchopneumonia with hemorrhage (aspiration). Focal atelectasis. Purulent otitis media, left.

Case 4. M.M. was admitted to the hospital on Feb. 22, 1947, 6 hours after her birth at another hospital. She was the 2nd child of an Rh-negative mother whose first born had been entirely normal. During the present pregnancy blocking antibodies in low titer had been discovered in the mother's serum. One week prior to the patient's birth, examination of the mother's blood revealed an anti-Rh titer of 1:64 in albumen. Labor was induced approximately 3 weeks before term and an apparently normal child was delivered. Re-examination 6 hours later disclosed the presence of jaundice. The infant was found to be Group O and Rh positive and the red blood cells were sensitized with blocking antibodies. Hgb. was 11.7 gm./100 cc. blood, RBC count 4.4 million, WBC count 70 thousand, platelets 320 thousand, and reticulocytes 4.5%. Differential blood count revealed polymorphonuclear cells 69%, lymphocytes 14%, monocytes 6%, eosinophiles 3%, basophiles 1%, myelocytes 6%, myeloblasts 1%. There were 25 normoblasts/100 wbc. Icterus index was 48 (acetone method).

A replacement transfusion was performed soon after admission. Through a plastic catheter introduced into the umbilical vein, 410 cc. of blood was removed and 595 cc. of group O, Rh-negative blood was replaced. Following this procedure 85% of the infant's cells were found to be Rh-negative. She remained in the hospital one week during which time the jaundice cleared. Hgb. at the time of discharge was 11.7 gm./100 cc. blood.

She did fairly well during the following five weeks but was then noted to have become moderately pallid. She vomited occasional feedings and her mother believed that she was febrile. There was no jaundice. She was readmitted to the hospital on April 3, 1947.

On admission she was well developed and nourished and did not appear to be ill. Temperature was 38.8° C. There was moderate reddening of the pharynx. There was pallor of the skin and mucous membranes. Liver and spleen were enlarged to 4 cm. below the costal margin. Hgb. was 6.5 gm. Urine analysis was negative and no bile was present.

Transfusions of 75 cc. of Rh-negative partially packed blood were administered on April 3 and 4 with a subsequent rise of Hgb. to 15 gm. and RBC to 6.88 million. On April 5 she was found to be lethargic and there was jaundice of the skin and sclerae. Abdomen was distended and the liver and spleen were enlarged as on admission. There was spasticity of the upper extremities and ankle clonus. She refused several feedings and vomited moderate amounts of "coffee-ground" fluid. Icterus index was 12 (acetone method), plasma chloride 99 m.Eq/l., CO_2 content 51.5 volumes per cent, and total protein 5.8 gm./100 cc. blood. Oral feeding was discontinued and she was treated with a continuous intravenous infusion of dextrose 5% solution to which were added vitamin B complex, ascorbic acid and penicillin. She seemed to improve for a short while but then the lethargy deepened, the jaundice increased in intensity and when small oral feedings were attempted, she again vomited brownish fluid. On April 8 the stools were noted to be tarry. She had become tachypneic and moist rales were heard throughout the chest. A prothrombin index was found to be 10% and repeated on the following day, there was no tendency to clot after 5 min. despite parenteral doses of vitamin K 2.4 mg. daily. The serum cholesterol was 120 mg./100 cc., with 60 mg./100 cc. cholesterol esters. The alkaline phosphatase was 36 King-Armstrong units; the cephalin flocculation was 3 plus.

The patient's condition continued to deteriorate rapidly. She was stuporous on April 10 with rapid stertorous respirations. Icterus deepened to a golden-yellow color. It was noted that the liver was shrinking in size so that the edge was just palpable at the costal margin. Icterus index rose to 99 and the serum bilirubin was 7.8 mg./100 cc. Respiratory stridor and dyspnea increased although direct visualization of the larynx failed to reveal any obstruction. Temperature rose to 39.5° C. on April 11 on which day she died.

Final diagnosis: Acute diffuse necrosis of the liver. Icterus. Hemorrhages into intestinal tract. Petechiae of pleura. Enlargement of spleen. Hemosiderosis of liver and spleen. Anemia. Acute bronchopneumonia (aspiration). Focal atelectasis.

Case 5. MV., a 6 month old male infant, was admitted to the hospital on February 9, 1947 with pneumonia of the right upper lobe which responded to treatment with penicillin. During his stay in the hospital he developed diarrhea. On February 23 he was noted to have become dehydrated and lethargic. Plasma CO_2 content was 27 volumes per cent. Patient was treated with a continuous

intravenous infusion of physiologic saline and the same day, 100 cc. reconstituted Red Cross pooled plasma was administered. He improved rapidly and was discharged from the hospital March 4. A supportive transfusion was given April 2 because of Hgb. 9.6 gm./100 cc. blood.

He remained well until March 25, 30 days after the plasma transfusion, when he became febrile and was seen by his private physician. There were no abnormal physical signs but his temperature ranged between 38.5° and 40.5° C. until April 1 when it was noted that he was jaundiced. He was admitted to another hospital where a diagnosis of infectious hepatitis was made. The following laboratory findings were reported (through the courtesy of Dr. Eisenoff): Blood icterus index 23, bilirubin 4 mg., and the cephalin flocculation positive 2 plus. Heterophile agglutination was 1:20. RBC fragility test was normal. Blood revealed Hgb. 10.0 gm./100 cc., RBC count 3 million, WBC count 13.8 thousand with polymorphonuclear cells 18%, lymphocytes 79%, monocytes 2%. Temperature subsided soon after admission and the jaundice cleared progressively. He was discharged from the hospital April 13.

Case 6. R.B., a 1 month old white male infant, was admitted to the hospital on January 28, 1947 with a history of severe diarrhea of 4 days' duration. On examination, there was marked dehydration and evidence of circulatory collapse. Liver and spleen were not large. The laboratory findings were: Hgb. 9.5 gm./100 cc. blood; hematocrit 33%. He was treated with a continuous intravenous infusion starting with M/6 sodium lactate and followed by dextrose 5% in Ringer's solution. A blood transfusion of 70 cc. was given on admission. Additional transfusions of reconstituted Red Cross pooled plasma were administered as follows: 75 cc. on January 31, 50 cc. on February 4, 50 cc. on February 7, and 70 cc. on February 23. Diarrhea was well controlled. He was discharged from the hospital on February 28, 1947.

The patient remained well and gained weight but on March 30, 1947, 30 days later, he was seen by a physician because he was unusually fretful. No explanation was found. A routine examination in April was said to have been negative, but when the infant was examined May 14 the liver was noted to be enlarged to 5 cm. below the costal margin and the spleen to 4 cm. below the costal margin. He was examined by one of us (S.K.) on May 16 and the hepatosplenomegaly was confirmed. However the infant was in good condition and had continued to gain weight well. Reexamination on June 16 revealed the liver and spleen to be of normal size and a cephalin flocculation test at that time was negative. Subsequent course has been uneventful.

Case 7. R.G., a 5½ month old white male infant, was admitted to the hospital on April 15, 1946 with a history of jaundice of about 6 weeks' duration. He was delivered one month prematurely by cesarean section on November 10, 1945. His mother had had severe symptoms of toxemia during the latter months of pregnancy. His birth weight was 1450 gms. but his neonatal course was uneventful except that two blood transfusions were given at four weeks of age because of anemia. He gained weight normally and left the hospital in December with a weight of 3050 gm.

He continued to gain well and remained normal until the first week in March 1946. At that time his mother noted that his skin was yellowish in color and there was a decrease in appetite. His stools were noted to be clay-colored. There was no vomiting or fever. During the following 6 weeks which preceded admission to the hospital, jaundice persisted but his stools gradually became normal in color. His weight gain was poor and his appetite was subnormal.

On examination, he was a poorly nourished, irritable infant who weighed 5,300 gm. There was no fever. There was moderate jaundice of the skin and sclerae. Abdomen was soft. Liver was enlarged to 5 cm. below the costal margin and the edge was felt to be firm and sharp. Spleen was enlarged to 4 cm. below the costal margin. The remainder of the examination was negative.

Laboratory examinations revealed Hgb. 9 gm./100 cc. blood and WBC 16 thousand with neutrophiles 58%. Blood urea N was 14 mg./100 cc., serum cholesterol was 180 mg./100 cc., total plasma protein 6.3 gm./100 cc., bilirubin 4.2 mg./100 cc. and blood sugar was 75 mg./100 cc. Glucose tolerance curve was normal. Urine showed a 2 plus reaction for bile, and urobilinogen was present in a dilution of 1:5. Bile was present in the stool.

During the first week in the hospital the patient's condition remained unchanged and his weight was stationary. A high protein, high carbohydrate, low fat diet supplemented with vitamins was prescribed. He took his feedings fairly well and did not vomit. April 24, his temperature suddenly rose to 39.5° C. and he appeared to be acutely ill. The jaundice had increased in intensity. There was marked anorexia and frequent loose stools. Roentgenogram of the chest revealed bronchopneumonia of the right upper and lower lobes. He was given a continuous intravenous infusion of dextrose

5% solution and, also, penicillin was administered intramuscularly. On April 25 and 26 his condition deteriorated rapidly. All feedings were refused and the patient vomited several times. There was a strong sweetish odor to the breath. He became lethargic and lapsed into coma. His temperature ranged between 41.5° C. and 42° C. The liver edge receded to the costal margin during this period and the patient died on April 26.

Permission for autopsy was not obtained. Laboratory examinations during the terminal illness revealed a blood sugar of 30 mg./100 cc., an icterus index of 50 (acetone method) and 120 (water method), and the cephalin flocculation 2 plus.

Unsuccessful attempts were made to trace the donors of the blood transfusions given in December at another hospital. Careful questioning of the family disclosed that the patient had not been in contact with any individual ill with infectious hepatitis.

Case 8. E.L., a 3 month old male infant, entered the hospital on February 25, 1948 with anemia, periostitis of undetermined origin and a diffuse bronchiolitis. The respiratory infection responded well to treatment but the etiology of the periostitis remained obscure. On February 28, Hgb. was 6.5 gm./100 cc. and a blood transfusion of 70 cc. was administered. He continued to improve and was discharged March 19.

He was readmitted 3 days later with an ulcerative stomatitis. Liver and spleen were felt 2 cm. below the costal margin. The oral and respiratory infection responded well to treatment with sulfadiazine and penicillin. During convalescence he contracted an acute diarrhea due to Pseudomonas aeruginosa (B. pyocyaneus) which was controlled with some difficulty. Fluids were administered parenterally and four transfusions of unpooled Group AB plasma and a blood transfusion were given between May 5 and 17. There were no apparent untoward reactions to any of these transfusions.

On May 24 the patient was noted to be icteric. A firm and nontender liver was felt 3 cm. below the costal margin. During the subsequent 16 days, there was a progressive increase in the degree of jaundice. The icterus index rose from 18 to 42 (acetone method) and the stools were acholic. Except for an initial rise in temperature to 38.5° C., he remained afebrile. His appetite remained good and there was a steady gain in weight on a diet high in carbohydrate, protein and vitamins and low in fat.

The urine contained bile and urobilinogen demonstrable in dilutions of 1:5 to 1:20. Blood count was normal. Cephalin flocculation reaction was 3 plus. Serum cholesterol ranged between 120 and 260 mg./100 cc. with an esterified fraction between 30 and 58%. Serum alkaline phosphatase varied between 19 and 26 King-Armstrong units.

During the 3rd week of jaundice, bile appeared in the stools in gradually increasing amounts. There was a progressive decrease in the icterus associated with an improvement in his physical status. He was discharged from the hospital 10 weeks after the onset of jaundice. When last seen, 1 month after discharge, he appeared well but his liver was still enlarged to 3 cm. below the costal margin.

Comment

The incubation period between the administration of plasma and the onset of clinical evidence of hepatitis in Cases 1 to 5 varied between 30 and 53 days, whereas in Cases 7 and 8 it was 3 months. In the experimental transmission of serum hepatitis to human volunteers by Neefe and his co-workers[19] and by others,[20] it had been demonstrated that the usual incubation period varied between 56 and 134 days. The extreme range recorded in the literature is from one to six months in contrast with the 17 to 43 day incubation for the parenteral transmission of infectious hepatitis. On the basis of the difference in the incubation period and other characteristics summarized in Table II (modified from Haven[21]), Neefe[22] differentiates between the etiologic agent of infectious hepatitis (IH virus) and that of homologous serum hepatitis (SH virus). The experimental data provide evidence that viruses SH and IH, although closely related, are not identical. It is also probable that there may be substrains of both and it has been suggested by some that the SH virus is a mutant of the IH type. Thus Francis[23] has shown that in a case of infectious hepatitis transmitted by the blood of a donor in the prodromal stage of

infectious hepatitis, the incubation period was 21 days. When the serum from this recipient was inoculated into human volunteers, it induced jaundice after 45 days. Since the IH virus can be transmitted by the parenteral route after a short incubation period, it can also be implicated in the production of a serum transmitted hepatitis and may have been the etiologic agent in some of our patients.

The quantity of blood or plasma injected does not appear to play any role in the

TABLE II

COMPARISON OF CHARACTERISTICS OF THE VIRUSES OF HOMOLOGOUS SERUM HEPATITIS AND INFECTIOUS HEPATITIS

	Serum Hepatitis	Infectious Hepatitis
Onset	Insidious; Low grade fever	Abrupt with fever
Incubation	56 to 134 days	17 to 43 days
Distribution of virus: Blood	During incubation and early stage; persistence duration unknown	During incubation and early stage; persistence duration unknown
Stool	Absent	Present
Nasopharynx	Unconfirmed	Unconfirmed
Urine	Absent	Unconfirmed
Immunity	Resistant to SH virus after recovery for at least 18 mo. Susceptible, perhaps increased, to IH virus	Resistant to IH virus after recovery for at least 1 yr. Susceptible to SH virus
Experimental transmission: Oral	No	Yes
Parenteral	Yes	Yes
Nasal	Unconfirmed	Not demonstrated
Protection by gamma globulin	Not demonstrated	Protection with 0.15 ml./kg, during incubation period

determination of either the length of the incubation period or the severity of the hepatitis induced.[24] Experimental studies have shown that parenterally injected quantities as small as 0.01 to 0.001 ml. of serum are sufficient to transmit the disease.[22, 25]

The high mortality of the cases in this series (5 of 8 cases) is at variance with the reported statistics, especially since it has been suggested that the disease is of a benign nature in children.[22] The mortality of the yellow fever vaccine cases in the United States was 0.2%.[26] In smaller series of cases, the mortality rates have been reported as between 2 and 19%.[22] It is likely that some strains are more virulent than others. There is also evidence to indicate that chronic dietary deficiency or the existence of other injuries before the onset of the hepatitis may increase both the susceptibility to and the mortality from serum hepatitis.[1, 2, 27] These may have been important factors in the increased mortality in the present series. It is also possible that the prognosis of this condition is worse in

infancy. The only two cases of serum hepatitis in infancy, observed by Benjamin and Simon[28] in Montreal, died with acute liver degeneration.

The clinical manifestations of serum hepatitis in infancy do not appear to differ markedly from the descriptions of the disease in adults. We noted that, as stressed by Neefe and others, [22, 26] it is impossible to predict the severity of the individual case. A patient with mild symptoms in apparent good condition may suddenly deteriorate and die within 24 to 48 hours. Thus all cases, regardless of severity, should be viewed as serious. Among the bad prognostic signs, previously noted by others[26] and also seen in these fatal cases, were the development of central nervous system signs, pernicious vomiting, an abrupt rise in temperature to high levels, petechial skin and mucous membrane hemorrhages, and a low blood sugar. Hepatomegaly was seen in all these cases, and the rapid decrease in the size of the liver was always associated with a deterioration of the patient's condition, and was an ominous sign in the five fatal cases. In four of the five fatal cases during the terminal phase of the illness the respirations became labored in character and were associated with inspiratory stridor which suggested obstruction of the airway. Direct visualization of the larynx was performed in one case and did not reveal any obstruction. At postmortem examination viscid secretion was usually found in the smaller branches of the bronchial tree. Marked hypothermia was a presenting symptom in two patients.

The regime recommended for the treatment of hepatitis is nonspecific in character.[22] Prolonged bed rest is an important factor in the management of adult cases. The diet usually recommended is one high in calories, high in carbohydrate and protein and low in fat. However, Hoagland et al.[29] could find no harmful effect from a diet relatively high in fat derived from dairy products as long as the protein intake was high. The value of vitamin supplements or the use of methionine, or choline and cystine is unproven. Grossman et al.[1] reported an apparent beneficial effect from the use of dextrose solutions 5 or 10% intravenously when feedings were refused because of anorexia. Turner et al.[26] state that, with the appearance of neurologic symptoms, no regime seemed to produce beneficial results. A diet high in protein, carbohydrate and vitamins and low in fat seemed to be of no avail in our cases. Methionine and choline were administered without effect.

The pathology of viral hepatitis has been well described in several recent reports, particularly those of Dibble et al.,[30] Lucke,[31] Wood[32] and Mallory.[33] The fatal cases here described were characterized by a striking uniformity of the pathologic anatomy which was identical with the descriptions of the fulminant cases of infectious hepatitis described by the above authors. There was diffuse and uniform shrinkage of the liver, which was flabby in consistence and was either yellowish-red or purple in color. The extent of the hepatic damage was usually not suspected by gross inspection. Histologically there was a catastrophic autolytic destruction of the entire liver with only slight variation in degree (Fig. 1). There was no evidence of regeneration of hepatic parenchyma and only slight proliferation of bile duct epithelium. In the central portion of the lobules, the site of the most severe hepatic destruction, there was a mild inflammatory reaction. There was a more marked inflammatory infiltration in the periphery of the lobules. The reticular framework of the liver remained intact (Fig. 2). Endophlebitis of the central vein was seen in one case (Fig. 3). In two of the cases there was extramedullary blood formation in the liver with good preservation of the immature blood cells. The absence of normal bile in the gall bladder was a conspicuous feature in three of the four cases. Marked

icterus, hemorrhagic phenomena and varying degrees of renal tubular degeneration was present in all four cases. There was only moderate enlargement of the spleen. A mild acute duodenitis and mesenteric lymphadenitis were present.

It is of interest to note that extramedullary hematopoiesis was not found in Case 4, an infant who had erythroblastosis fetalis at birth and who had been treated with a replacement transfusion. The severe hepatic destruction found at autopsy cannot be related to the lesions described by Rosenblatt[34] in infants similarly treated with replace-

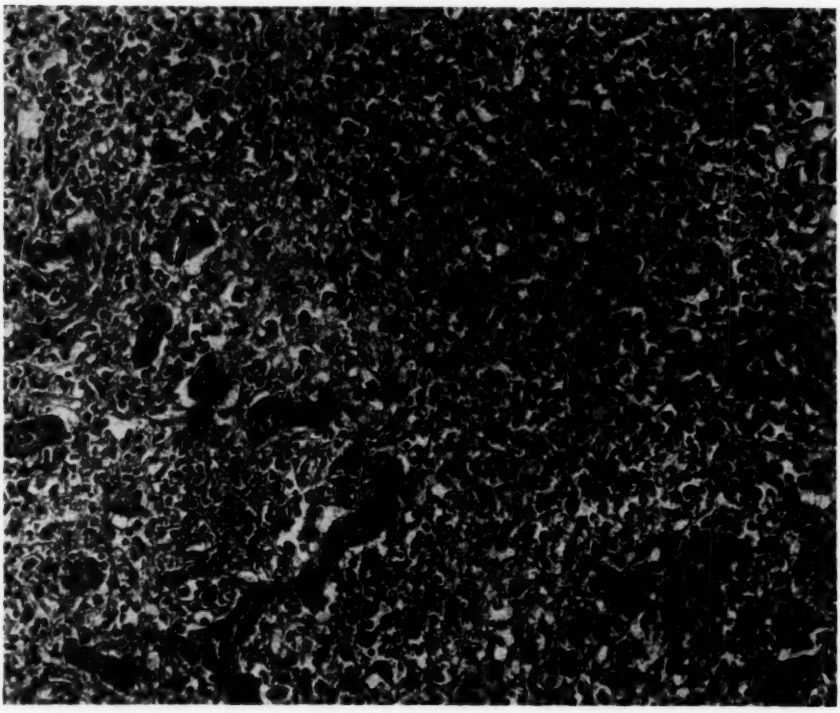

FIG. 1. Massive autolytic necrosis of liver parenchyma. Destroyed lobule is invaded by macrophages and inflammatory cells. At periphery of lobule there is some proliferating bile duct epithelium. x175

ment transfusions. Hepatic injury in his cases followed transfusion within one to five days, whereas there was an incubation period of 40 days between the transfusion and the appearance of jaundice in this case.

The prevention of homologous serum hepatitis is a major problem in view of the increased utilization of blood and plasma and the resistance of the etiologic agent to usual antiseptics and processing methods. As yet there are no means available for the detection of infective blood, plasma or serum except by transmission to humans. It has been demonstrated that the administration of human gamma-globulin to persons exposed to infectious hepatitis during the incubation period before the onset of symptoms may afford complete or almost complete protection.[35] However, the efficacy of gamma-globulin in the prevention of serum hepatitis has not been demonstrated.[1] Case 1 in the present

paper had received gamma-globulin as a prophylactic agent against measles without any beneficial effect upon the hepatitis which appeared eight days later.

Oliphant[36] demonstrated that the serum hepatitis virus was destroyed by exposure to ultraviolet light of 2650 Å for one hour and for 1½ hours to 2537 Å. Wolf et al.[37] studied the Oppenheimer-Levinson method for rapidly sterilizing suspensions of bacteria and viruses by exposing rapidly flowing thin films of liquid for fractions of a second to a powerful source of ultraviolet light. They determined that plasma treated in this

FIG. 2. Intact reticular framework of liver. It is collapsed and sinusoids are dilated. (Goromi's silver stain for reticulum.) x175

fashion could be administered without reactions. However there are no reports on the effect of this method upon infected plasma.

The substitution of human serum albumen for whole plasma transfusions may prevent the incidence of serum jaundice when sufficient quantities of this material become available at a lower cost. It has been shown that stabilized preparations of albumen may be heated for 10 hours at 60° C. with inactivation of the virus of serum hepatitis.[38]

For the present the suggested methods[5, 6, 10] for the control of serum hepatitis include: 1. Donors should be excluded who have a history of jaundice or contact with infectious hepatitis, or a history or having received human blood or products within a year. 2. Greater efforts should be made to detect donors with the prodromal symptoms of infectious hepatitis by a more thorough history and physical examination and possibly a spot urine test for the presence of bile. 3. Since the likelihood for contamination of a

pool of plasma is augmented by an increase in the number of contributing donors, either small pools should be used or else the practice of pooling plasma be discontinued. 4. Whenever indicated and feasible, whole blood should be used in preference to pooled plasma. 5. All syringes, needles and other equipment used for parenteral treatment or for the withdrawal of blood should be properly sterilized by boiling for 15 to 30 minutes or by autoclaving.[39] 6. All blood products should carry identification data and records should be kept of the contributing donors. 7. The lot numbers of blood products should

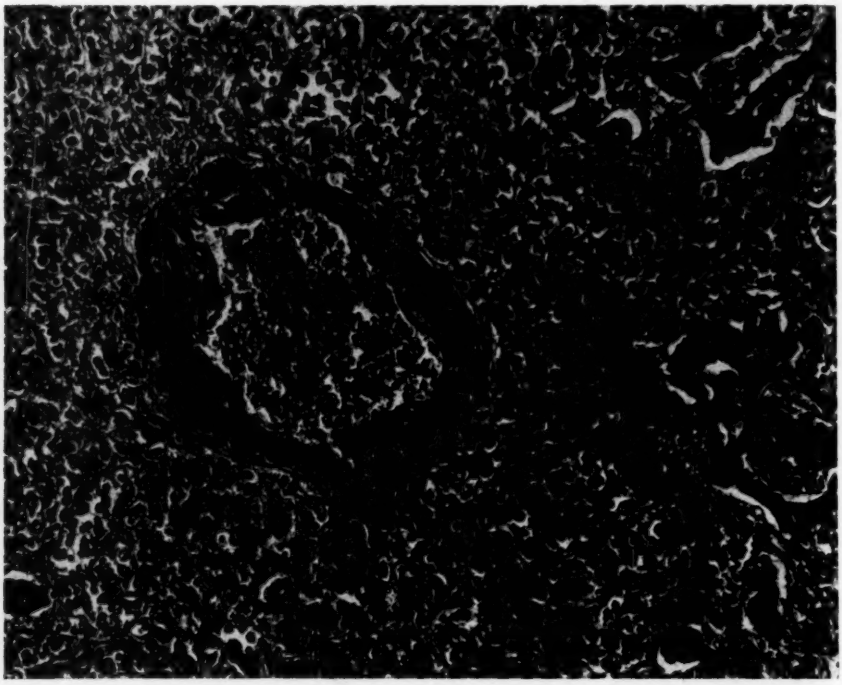

FIG. 3. Case 1. Endophlebitis of central vein. Wall has smudgy staining reaction. Central part of lobule is completely destroyed. Marked inflammatory reaction at periphery. x175

always be recorded on the recipient's chart. 8. If the latter two methods are effectively carried out, the known icterogenic lots can be removed from distribution. 9. Finally, the transfusion of blood or plasma should be given only for definite indications.

SUMMARY

Eight cases of homologous serum hepatitis are reported as having occurred in seven infants under one year of age and in a child of 2½ years.

Five of these children died of acute hepatic degeneration.

Suggestive evidence has been presented for the implication of icterogenic plasma in five cases.

The clinical, laboratory and postmortem findings of serum hepatitis are described in detail.

Preventive measures have been reviewed and summarized.

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SPANISH ABSTRACT

Hepatitis de Suero Homóloga en Infantes y Niños

Se reportan ocho casos de hepatitis de suero homóloga que ocurrieron en siete infantes de menos de un año de edad y en un niño de dos años y medio de edad. Cinco de estos ninos murieron de degeneración hepática aguda. Se ha presentado prueba que sugiere la complicación de plasma icterogénica en cinco casos. Se describen en detalle los descubrimientos clínicos, de laboratorio y los que se hicieron después de la muerte. Se han revisado y resumido las medidas preventivas.

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Pediatrics

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AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

REPORT OF THE FIRST MEETING OF THE SECTION ON SURGERY OF THE AMERICAN ACADEMY OF PEDIATRICS

The first meeting of the Section on Surgery of the American Academy of Pediatrics was held in the Chalfonte-Haddon Hall Hotel, Atlantic City, N.J., on Nov. 21, 1948. Those present were: charter members of the Section—Drs. W. E. Ladd, H. E. Coe, O. S. Wyatt, J. R. Bowman, F. D. Ingraham, C. E. Koop, T. N. Lanman, J. Lozoya, W. J. Potts, and Henry Swan, Jr., and guests—Dr. Fontana of Montevideo and Dr. Clifford Sweet.

The Chairman reported that the Executive Board of the Academy had approved the following as charter members of the Section in addition to the 10 present: Drs. A. H. Bill, Jr., F. Cachof, T. C. Chishold, R. E. Gross, J. M. Moore, W. T. Mustard, D. W. MacCollum, C. Serinanan, Orvar Swenson, and F. R. Wilkinson and the following policy, or steering, committee: H. E. Coe, chairman, and C. S. Wyatt, to serve three years, R. E. Gross and J. Lozoya, to serve two years, and W. E. Ladd and Henry Swan to serve one year; two members are to be appointed for a three year term each year hereafter, each member being eligible to succeed himself only once.

Dr. Coe then outlined briefly the history of the development of the Section:

1. Surgical subjects have been presented at meetings of the Academy by round table discussions at intervals over a period of some 15 years.

2. Constant expansion of the fields of activity of the Academy.

3. A plan for including children's surgery in Academy activities was presented formally to the Executive Board at the Detroit meeting in 1945.

4. The proposal was studied, reported at the meeting in Pittsburgh early in 1947 and a committee appointed consisting of Drs. Beaven, Ratner and Coe to consider enlarging the membership to include those in allied specialties whose work is limited to the care of children.

5. The report of the Executive Board recommending this expansion of membership was approved at the Dallas meeting in 1947 and the Committee was directed to collect and present further data. The Dallas meeting was the first at which an entire section of the program before the Academy was devoted to surgical conditions.

6. The Committee studied conditions in Canada, the United States and Mexico, formulated necessary changes in the constitution and by-laws and reported at the meeting of the Executive Board in July 1948.

7. The Board took action including:

The formation of three sections: Allergy, Surgery, and Mental Growth and Development.

The appointment of a steering, or policy committee for each section.

The authorization of appropriate application forms.

Determination of Composition of the sections and roster changes.

Limitation of the surgical section to 20 charter members whose practice should be not less than 90% children's surgery.

Elimination of an initiation fee for those approved for membership in the Section on Surgery, fixing the dues at one half the usual annual dues, and adding the $10 Journal fee, making the annual payment for those newly admitted to the Academy $25.00.

8. The Executive Board at a meeting preceding the Atlantic City meeting in 1948 approved the admission to membership in the Section on Surgery of the 14 applicants who were not already members of the Academy.

On motion duly made and seconded, Dr. W/m. E. Ladd was unanimously elected Honorary Life President of the Section.

The remainder of the meeting was devoted to informal discussion of interesting and pertinent aspects of children's surgery and the relationship and obligations of the Section to the Academy. Dr. Ladd opened the discussion by pointing out the necessity of the closest cooperation between the members of the Section and the Program Committee in order to further the objectives of the Academy in providing the best possible care of children. One of these Section members might well be on the Program Committee or working in close cooperation with that Committee in order to facilitate the presentation of the surgical aspects of any appropriate subject. Surgical papers should deal with subjects of general interest to the entire membership of the Academy and should emphasize diagnosis and pre- and post-operative care rather than operative technic. Common disorders should be featured rather than rare or spectacular conditions. The presentation of such papers would assist in promoting the educational program of the Academy, the discussions being of value to medical and surgical pediatricians alike, thus raising the standard of children's surgery, and improving the care of children generally. Meetings of the Section for technical discussions might be held separately either before or during the general meeting but should be open to all interested members of the Academy.

The need for better undergraduate instruction in pediatric surgery was discussed and Dr. Koop pointed out the advisability of channeling recommendations through the Academy's Committee on Pediatric Education.

The question of expansion of the Section was discussed. Dr. Ladd expressed the opinion that we should be very careful about recommending the addition of more members for the present until policies can be more thoroughly developed.

Dr. Lozoya told of two or three young surgeons in Mexico who are doing excellent children's surgery exclusively and who would be desirable additions to the Section. The concensus of opinion was that any candidate for membership should be certified by the American Board of Surgery or have qualifications which would make him eligible for such certification. It was felt desirable that a procedure should be developed for considering applicants whereby they would be approved by a pediatric committee as well as by a committee of this section before their names are submitted to the Executive Board. The submission of the names to the fellows of the applicant's district in the same manner as for other applicants for fellowship would perhaps be sufficient pediatric endorsement.

The question of necessary training for the practice of children's surgery arose in relation to requirements for certification by the American Board of Surgery. It was felt that the requirements for the practice of children's surgery should not be the same as for the practice of general surgery, the latter requiring a disproportionately long training in conditions never or only rarely encountered in children. The children's surgeon should have at least one year general internship, a year basic science which could possibly include pediatrics, two years of general surgery, and two years of children's surgery. Dr. Potts stated that the American Board of Surgery will accept only one year of children's surgery and he considers the training period required by the Board unnecessarily long. Dr. Ingraham advised a more rational distribution of time and subjects but stressed the necessity of maintaining a high standard. Dr. Potts felt that the training should include two years of general surgery or its equivalent and two years of children's surgery. It was decided to place the problem before the American Board of Surgery for discussion and because of Dr. Lanman's position on the American Board and Dr. Ladd's intimate acquaintance with members of the Board, these two be requested to discuss the subject with the Board and report at the next meeting. It was suggested that a Board of Pediatric Surgery as a subsidiary of the American Board of Surgery might possibly be

a future development if growth of the specialty should warrant it, but that there is no immediate necessity for considering this.

Dr. Lozoya spoke of the resident training for Mexican surgeons in the United States which has been available for a few hospitals at times over a period of several years. He feels that this should be continued and developed not alone for the professional value to the resident but for broadened education of all concerned and furtherance of international understanding and friendship. He mentioned the value of exchange residencies, and commended the assistance granted to deserving individuals by subsidies from the Mexican Government, and fellowships from the Kellogg Foundation through the Academy, and from the Mead Johnson Fellowship Committee on Pediatrics Research for the Latin American countries.

Dr. Lozoya extended a most urgent and cordial invitation to members of the Section to attend and participate in the surgical section of the Pan-American Pediatric Conference in Mexico City, November 2-5, 1949, preceding the San Francisco meeting of the Academy.

GRADUATE EDUCATION FOR PEDIATRIC PRACTICE

By JOHN MCK. MITCHELL, M.D.

In 1947 the Study of Child Health Services of the American Academy of Pediatrics* conducted a survey of the hospitals approved for residency training by the American Board of Pediatrics and the Council on Medical Education and Hospitals of the American Medical Association. This paper is concerned with an appraisal of the training provided in these hospitals, with special reference to the manner in which this training meets the prescription of the Board, which defines service "as full time devoted to rounded experience in an approved hospital which includes ward and outpatient service, experience with newborn, including premature and both therapeutic and preventive pediatrics."

In general it may be said that the Study demonstrated that almost all approved hospitals are fully cognizant of their role as educational institutions and are making a conscientious effort to provide a thoroughly acceptable training program. Further, that training in the diagnosis and medical care of the sick infant and child is generally excellent. In certain special categories, however, the situation is not so uniformly satisfactory. The fact that these deficiencies are stressed in this paper must not be taken as an indictment of residency training programs as a whole, but rather as constructive criticism aimed at the strengthening of weak spots.†

In 1947 there were 180 hospitals approved for residency training in pediatrics, of which exactly one half were connected with departments of pediatrics in the medical schools. The remainder represented those hospitals whose pediatric services were of sufficient competence to warrant recognition as training grounds for pediatricians.

In a detailed study of 158 of these hospitals the total resident staff numbered 843 physicians, divided as follows:

Total Resident Staff	843
Straight Interns	187
Assistant Residents	450
Residents	206

In addition to the 187 straight interns listed above, that is, interns devoting an entire year to pediatrics, there were 253 rotating interns who served for a period of a few weeks to six months. Hence there were a total of 392 interns serving on pediatrics at a given time. On the basis of the period of time served by these rotating interns, it can be estimated that approximately 2300 physicians receive pediatric intern training annually in hospitals approved for pediatric residency training. In 1947 there were 5678 graduates from medical schools in the United States. Therefore, only about 40% of graduates receive any pediatric training in hospitals approved for residency training in that field.

Size of Pediatric Service

One measure of the value of a given residency is the amount of clinical experience gained by the incumbent.

Among the 158 hospitals studied, 7 have less than 25 children's beds. There are 40 hospitals training 387 residents annually, in which there are less than 250 annual child admissions per resident. The actual average is less than one admission per resident every 2½ days.

This would seem to indicate a definitely insufficient case load, though it must be admitted that the figures do not represent the situation with complete fairness. Among the 387 residents are included

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Read before the Annual Meeting of the American Academy of Pediatrics, Atlantic City, N.J., Nov. 21, 1948.

* Much of the material which is contained herein is taken from the "Study of Child Health Services" which has been published by the Commonwealth Fund, and is presented here with their approval.

† The author of this article is not a member of the American Board of Pediatrics and opinions expressed do not necessarily represent the views of the Board.

129 straight interns, and in many hospitals which grade the responsibility of their house staff, an intern and an assistant resident are both assigned to a given case. On the other hand the figures exclude rotating interns whose relative number would alter materially the work to be performed by the assistant resident or resident. To complicate the situation still further, in many hospitals a portion of the resident staff will be absent on rotation or perform outpatient service on a full time basis for a certain part of the year.

Care of Newborn and Premature Infants

There are grave difficulties encountered in giving undergraduate medical students clinical training in the care of newborn and premature infants. Many factors combine to hold to a minimum the contact between newborn infants and undergraduate clinical clerks. As a result it is of special importance that the residency training program should provide a maximum of experience in the handling and care of the newborn infant. The fact that there are 20 hospitals in which 93 residents receive no training in their care, therefore, becomes a matter of deep concern. It offers an indictment of the completeness of the training program in these hospitals which cannot be dismissed lightly.

In addition there are 21 hospitals (15 teaching and 6 nonteaching) in which the pediatric department does not have direct control of the nurseries, but in which the pediatric resident staff does obtain some experience in newborn care. In some of these hospitals the training is equivalent to that obtained in those under direct control, but in others it consists merely of occasional consultant services.

In view of these deficiencies, it is reassuring to find that the 117 hospitals which offer experience through direct pediatric control of newborn infants account for the training of 581 residents annually. It should not be assumed that all of the remaining 262 residents receive inadequate training. In addition to the group already mentioned, who receive adequate training in newborn services although these are not under direct control, many of the remainder do not stay in one hospital for their entire residency period. Still others have received some experience during rotating internships. Others, realizing their own deficiency, take short appointments on maternity services.

The situation with regard to training in the care of premature infants is more favorable than that for the newborn. This is explained by the fact that practically all children's hospitals and some pediatric services in general hospitals which do not provide newborn experience, have units for the care of premature infants. As a result only 7 hospitals provide no experience in premature care and these hospitals train only 32 residents annually. There are 8 other hospitals in which the residents receive training, although the premature infants are not under direct control of the pediatric staff. In many hospitals, however, the amount of experience gained in the handling of premature infants is very small.

In all there are 5 hospitals which provide no experience to their 26 residents in the care of either newborn or premature infants.

Contagious Disease Training

Of the 158 hospitals studied, 83 hospitals provide formal contagious disease experience for the resident staff. In 22 instances this experience is obtained by rotation through other hospitals or through other services in the same hospital. Although only half of the hospitals have isolation units, about two thirds of the resident staff (567) receive their training in these hospitals.

It should not be inferred that all of the other third of residents receive no experience in the care of children with contagious diseases. Some hospitals without isolation units admit a considerable number of patients who would be referred to such a unit if one were available. Indeed the border line between the type of cases admitted to hospitals with small isolation units which are physically essentially a part of the service proper, and cases admitted to hospitals lacking any formal isolation unit, is so fine as to be almost nonexistent. It is the strong belief of the writer that, in both categories, there are a number of smaller services which do not admit contagious disease cases in sufficient number and variety to provide adequate experience in this field to the very considerable number of residents who receive all of their training in these hospitals. It is not possible to support this opinion with figures on admissions by diagnosis, but it is based on wide personal observation of the range of cases found on the wards of these hospitals, and on conversations with the residents on these services.

It is true that many of the hospitals which fail to provide contagious disease experience are found

among those which are approved for only one year of residency training, but many are approved for two years. Moreover, it is common practice for residents to move from one hospital approved for a single year, to another hospital approved for a similar period.

It is believed that this deficiency in contagious disease experience could be removed in large measure by the adoption of one of several possibilities which present themselves. The most obvious of these is through affiliation with a hospital having a contagious disease service. The Board allows six months' credit for residency training in hospitals which confine their admissions to patients with contagious disease. This makes it difficult for such hospitals to obtain residents for a full year. In addition, there are many contagious disease hospitals and services which might have difficulty in obtaining approval for residency training in their own right, but which would be satisfactory for such experience on an affiliation basis. This solution is proposed in full cognizance of the trend toward the abolition of separate contagious disease hospitals and in spite of complete sympathy with the desirability of integrating the care of contagious disease patients with general medical pediatrics. The fact remains that today, many separate hospitals exist and that the patients cared for on these services are not utilized to the best advantage for residency training purposes.

A second solution lies in the pediatric service of the hospital undertaking the medical care of children in orphanages, foundling homes and other institutions of this sort. Through affiliation with such institutions it is possible to offer the resident a considerable experience in the minor contagious diseases which he is apt to miss on his regular hospital service. Some hospitals utilize this method but the number is small.

A third means of broadening training in this field is through the development of domiciliary care programs. Only six hospitals had well developed home care plans in 1947 and these did not necessarily include every resident. Two more hospitals are known to have been contemplating this step.

Training in the Care of Children with Surgical Conditions

It is essential that the pediatrician be thoroughly trained in surgical diagnosis. In the case of infants and small children, good preoperative and postoperative care are of primary importance to a successful outcome in every major surgical procedure. The pediatrician must assume his share of the responsibility, which not infrequently is left entirely in his hands.

The volume of minor surgical conditions cared for by pediatricians varies greatly. In private practice, some pediatricians personally treat a large number of minor surgical cases, while others refer all but trivial accidents to other physicians. In any event, only through hospital training can the pediatrician acquire the necessary skill in surgical diagnosis and a full appreciation of the possibilities and limitations of surgical procedures.

In view of the importance of surgical training, it is gratifying to find that experience in this field is afforded by 133 of the 158 hospitals and that these hospitals account for 87% (732) of the residents in training in a single year.

Outpatient Training

Ample experience in a well-conducted outpatient service is an essential feature of a rounded residency training program. The problems presented to the resident in the outpatient department are identical with those which will confront him in practice. The manner in which these problems are approached and handled establishes a pattern which will influence profoundly his future practice. The pediatrician who enters practice without adequate experience in outpatient procedure is indeed handicapped.

There are 16 hospitals which offer no general pediatric outpatient service or less than 50 hours in either the resident or assistant resident year. Seven of these hospitals have no outpatient department at all. Four hospitals have this service available but provide less than 50 hours of training. In the remaining five hospitals an outpatient department is available but training is confined to the intern year. These are all large hospitals with ample outpatient facilities and large house staffs. Assistant residents are usually chosen from among their own interns. The fact that outpatient service is performed during the intern year and not in later years therefore becomes a matter of internal administration. However, in two of these hospitals all internships are rotating, hence the amount of training received is small. Moreover, the wisdom of restricting outpatient experience to the intern level of training is open to question.

Summary

This paper has concerned itself only with the availability and utilization of facilities in certain major fields of the residency training programs of approved hospitals. Many items of importance have been omitted for the sake of brevity. This indicates no lack of appreciation of their role in a well-rounded experience. A discussion of these features will be found in the Academy report, "Child Health Services and Pediatric Education." Brief mention of the more significant factors may serve to show the great range of experience needed to fulfill the requirements of a graduate training program complete in all respects. Thus, it is difficult to overestimate the influence of an active research group. The teaching value of organized ward rounds and well-conducted clinical conferences and seminars must not be overlooked. Training in the clinical laboratory, in pathology and radiology, in the accident and admitting ward must be included. Experience should be offered in the care and feeding of well infants; in preschool and school health services; in the training of the handicapped child; in convalescent care. Skill in the handling of children with incipient or already developed psychiatric disorders is essential to the proper conduct of a pediatric practice. Nor should the well-trained physician be unaware of the importance of social, economic and environmental factors in their relation to disease and the role of the social service worker in uncovering and solving these problems.

Even with the omission of a discussion of the presence or absence of these features in this paper, it is believed that sufficient evidence has been presented to demonstrate that grave deficiencies exist in the training of residents in many hospitals. These deficiencies may be recapitulated briefly as follows:

	Total hospitals—158 Lack training		Total residents—843 Amount of training questioned	
	Hospitals	Residents	Hospitals	Residents
# admissions per resident	0	0	40	387
Care of newborn	20	93	21	169
Care of premature	7	32	8	37
Contagious disease training in isolation unit or hospital	75	276	17	69
Surgical training	25	111	0	0
Outpatient training	7	15	6	29

In addition to the 158 hospitals shown in these figures there were 22 hospitals approved for residency training in pediatrics in 1947. The majority of these hospitals received their approval too late in the year to be included. Most of the remainder were isolated institutions. Practically all were smaller hospitals, which patently find it more difficult to provide a service complete in all features. Therefore, it is highly probable that if data concerning these 22 hospitals were added, the number of deficiencies listed above would be increased materially.

A large number of hospitals are currently seeking Board approval for residency training. Very few of these hospitals are associated with medical schools. A majority of them represent small pediatric services which cannot hope to offer the type of experience available in the major teaching centers and large, well-organized children's hospitals and departments which have been the graduate training ground of the vast majority of pediatricians certified in the past.

Meanwhile, the demand for residency appointments in pediatrics exceeds the supply, although there is evidence that the peak of the war-created backlog has been passed and that the situation is stabilizing. Due to the recent demand, however, many hospitals have been stimulated to seek approval. The Board is under constant pressure for action by these institutions. Unfortunately, the Board is not in a position to undertake the immediate personal survey of every hospital which applies, although this would be highly desirable.*

Consideration of the factors presented introduces decisions of policy which will affect the caliber of pediatric practice for many years to come. Every hospital which is now approved should arrange to supply those features in which it is deficient. The approving agencies should make certain that

* The Council on Medical Education and Hospitals conducts a separate survey.

every hospital which is accepted for residency training in the future should have available or should supply by affiliation, complete facilities for a training program that omits no feature essential to the experience of the practicing pediatrician.

Criticism has been leveled at the Board for its general residency training requirement. This criticism is usually based on the contention that some physicians seeking Board certification do not plan to practice pediatrics. Even so, there is good reason to believe that this period of clinical experience will prove to be of great benefit. Further, there is no means by which it can be guaranteed that any holder of a Board certificate will not enter the practice of pediatrics. Meanwhile the Board has a definite obligation to its own diplomates, to other physicians and to the public, that the recipient of its certificate shall have received training which fits him to meet all of the demands of practice.

An urgent plea is made to the staffs of approved hospitals that they take immediate steps to correct existent defects of which they must be aware. Attention is again invited to the great possibilities offered by the plan of affiliation with other institutions, as a means of supplying deficiencies which cannot be met within the hospital itself. Since residents may spend several months in the accessory service, it is not necessary that the two hospitals should be in the same community.

The favorable position which pediatricians hold in this country today is due, in a large measure, to the relative excellence of the graduate training which has been offered in the past. Unless this high level is maintained, there is real danger that the pediatrician of tomorrow will find himself in a far less enviable position.

FINANCIAL ASPECTS OF PEDIATRIC EDUCATION

By JOHN P. HUBBARD, M.D., AND JOHN McK. MITCHELL, M.D.

A year ago we presented at the Annual Meeting of the Academy some of the findings that were beginning to emerge from the Study of Child Health Services. This comprehensive nation-wide survey is now complete and in publication.[1] One of the most important aspects of this study is the fact that it has coupled with a study of services an evaluation of the training of those who are rendering the services.

Many members of the Academy participated in the collection of information from practicing physicians, hospitals and community health agencies. The results of these inquiries are now in the hands of state chairmen who are reporting the findings for their own areas. These state reports which are appearing in increasing number contain not only a summary of the data but also include recommendations as to what ought to be done within the state to fill existing gaps and to improve the health of children.

But the information on pediatric education is less familiar to the many who participated in state programs. This part of the study was necessarily conducted from a central office with one of us, Dr. Mitchell, making a personal visit to each of the 70 approved medical schools and nearly all of the hospitals approved for pediatric residency.

Now that we have reached a point where we can see the whole picture, the Study of Pediatric Education appears in a place of prominent, if not dominant, importance. Service is, after all, a dynamic function, and can be only so good as the training, skills and abilities of the individuals who give it. In the last analysis, good medical care for children depends not so much on the physical facilities of the hospitals or the expansion of health services as upon the judgment and skill of physicians. This skill is the result of training and experience. It was this very fact which at the outset led to the inclusion of an evaluation of pediatric education and which now appears as the logical starting point for a program for the improvement of child health.

Of the many aspects of pediatric education, which will be discussed fully in the published report, the gross inadequacy of pediatric department budgets has been selected for review at this time.

It should be kept clearly in mind that pediatric education is only a part of a far larger and more difficult problem facing medical education in general. We are not unaware of the broader dimensions of the problem but have confined our discussion to this part of the situation in which we have had some experience and in which we now have a large body of factual information.

The medical school budget as a whole will be considered first. In any analysis of these budgets it is important to bear in mind the different methods of bookkeeping and the many other factors which vary from school to school. A share of administrative costs of the university may or may not be included in the medical school budget. Interest and amortization charges may or may not be carried as a building upkeep item. Schools of nursing, public health and dentistry may share buildings and faculty with the medical school. Grants for research often are made directly to departments; some schools make no accounting of these sums, while others include them in their budget.

Correction for these differences is simple when compared with an effort to unscramble medical school and hospital costs. The medical school uses the plant of the hospital for teaching purposes. Some schools pay the hospital for this privilege; most do not. Medical school faculty and hospital staff are freely intermingled. The salary of physicians comes sometimes solely from the medical school, sometimes entirely from the hospital, sometimes from both, and not infrequently physicians receive no pay for the teaching they do. Remuneration which comes from the hospital is rarely shown as an item on total medical school budgets, while it appears regularly in departmental budgets.

With these variant factors in mind it may be stated that on the basis of figures gathered during this study for the 70 approved medical schools in the year 1946-47 the total gross budgets of these schools was in the neighborhood of $45,000,000. For the same year the American Medical Association reported[2] a total of $43,000,000 for the medical schools including seven schools of basic medical sciences. The difference between this figure and ours may be attributed largely to the inclusion of certain research grants in our estimate. In comparison with the overall gross budget for the 70

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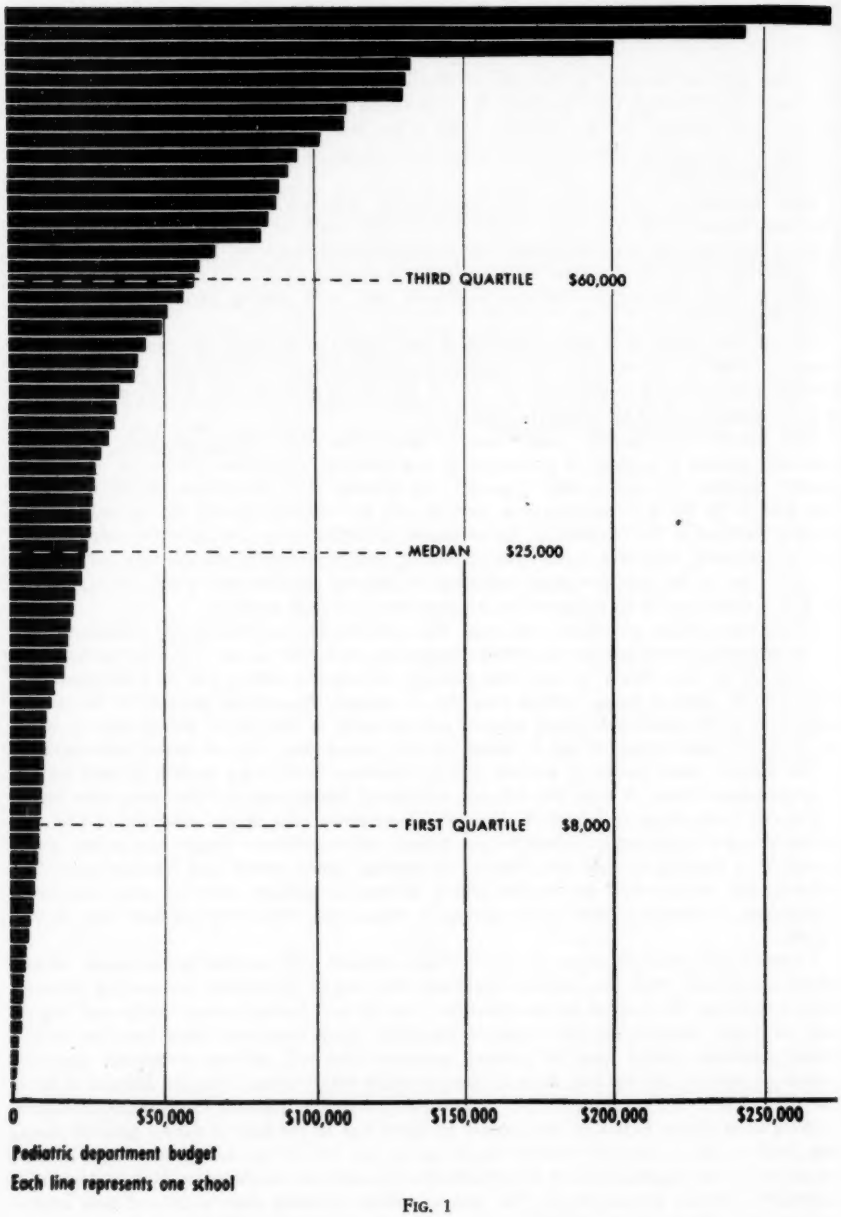

FIG. 1

medical schools, the total of the budgets of all pediatric departments for the same year was approximately $3,000,000. This sum includes payment made to members of the department by hospitals. Remuneration to bacteriologists, chemists, pathologists, roentgenologists and others not on the pediatric staff is excluded.

Figure 1 shows graphically the pediatric department budgets of the 70 medical schools. Each bar represents one school. It is very evident that there is a wide range between those with the larger budgets and those with the small budgets. There are nine schools with budgets of $100,000 or more. Half of the schools have a budget less than $25,000. Twenty-one departments have budgets less than $10,000 and 11 less than $5,000 annually.

In Figure 2 we have shown the sources of income from the pediatric department as a whole and separately for teaching, research and other purposes. Pediatric departments receive only half of their

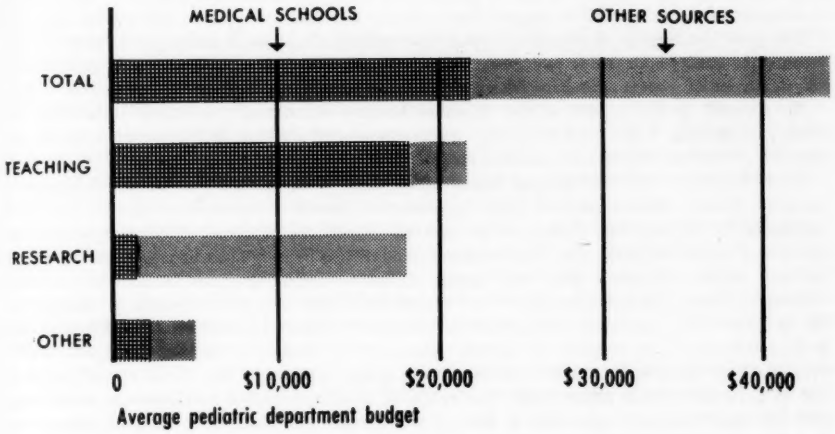

FIG. 2

total income directly from the medical school. Included in the other half of the budget are grants, both government and nongovernment, department endowment, and income from hospitals and other sources. The department funds allocated to teaching are derived almost entirely from the medical school. On the other hand, research is supported almost entirely by outside grants. The schools provide about half of the funds used for general expenses but these funds represent only about 10% of all departmental expenses.

Funds from government sources supply approximately 6% of the total departmental budget exclusive of appropriations for general expenses. Most of these funds from government grants go into research. Grants which come from individuals, foundations or commercial firms are often given for specific purposes. They are apt to be a single donation covering a given project for a limited period of time. They represent an extremely important item in pediatric department budgets, accounting for 24% of the grand total and one half of all money spent on research. Hence, any material decrease in these sources of revenue, whatever the cause, would represent a most serious problem to many of the largest and strongest pediatric departments and virtually wipe out some of the smallest departments.

Furthermore, it is important to bear in mind that decrease or withdrawal of research funds would have a very marked effect upon the teaching program. In addition to the favorable effect which a research program exerts, many members of the research staff are essential to the teaching program, although their salaries are derived from research funds.

An item which is perhaps of even more immediate interest is the source of income for those who are teaching pediatrics. In the 70 medical schools there are 460 pediatric staff members, exclusive of the resident staff, who give at least one quarter of their time to teaching (500 or more hours per year). Approximately one fifth of this group derive their entire support from private practice. Significant as this figure may be it tells only part of the story. Half of the staff members serve on a part-time basis. The salary that they receive from the medical school or hospital is usually small, often only a token, and does not represent an appreciable contribution to their income. In reality they too are dependent upon private practice for their support. These figures do not include an additional 900

teachers of pediatrics who give less than one quarter of their time to teaching; 84% of this group receive no pay for the teaching they do. If this large group of less than one quarter time teachers who receive no pay for their services should be withdrawn, pediatric teaching would be seriously handicapped.

At a reasonable estimate there would be no department of pediatrics in 28 schools if it were not for these physicians who give their time and energy with little or no pay in order that medical teaching may go on. Not included in this number are six schools in which all the key members of the pediatric staff earn their own pay by practice based at the hospital. Another five schools count on a strong children's hospital to support their pediatric staff and five more do this in large measure.

The gross inadequacy of financial support for medical education is being given much serious attention by many, both inside and many outside the medical profession. From many quarters we hear discussion of what is termed the crisis facing medical education.

An editorial in the Journal of the American Medical Association[3] has stated "unless there is general recognition of the need for more adequate support of medical schools, deterioration of the standards of medical education and medical research will ensue."

More recently, in the 1948 Annual Report of the Council on Medical Education and Hospitals, American Medical Association,[4] the following statement appears: "The medical schools are almost unanimous in declaring that if they are to continue to meet the problems of inflation successfully and if they are to undertake new developments, important to their fundamental programs of undergraduate medical education, they will require additional operating funds in addition to those currently available. About four-fifths of the schools were able to furnish estimates of their needs. On the basis of the figure submitted, it can be estimated that the additional funds needed by all the medical schools amount to about $15,000,000 annually." It should be emphasized that this sum of $15,000,000 is stated as the annual requirement for operating expenses. The report just quoted gives also an estimate of nearly $200,000,000 required by 55 schools for capital developments. A university president who has given a great deal of thought to the problem of financing medical education wrote in a letter published in PEDIATRICS:[5] "The future of medical care, including pediatric care, lies in the training of physicians to provide that care for the people of our nation. That training, in proper quality and in necessary numbers, depends upon the prosperity and quality of American medical schools. Financially, the situation of many of those schools is perilous, and the situation of some of them is desperate."

There is no argument as to the need, but there is much lively discussion as to the ways and means to meet the need. Some feel that contributions from voluntary sources can be raised in sufficient quantity; others feel that since so much of the money formerly available from voluntary sources is being drained off by taxation, a larger proportion of the Federal dollar should be returned to support medical education. Some schools are contemplating an increase in tuition. In this paper we do not intend to evaluate the comparative merits of methods of meeting the need; we are concerned only with a review of the facts in regard to the financial aspects of pediatric education today.

In this connection it is of particular interest to note the extent to which the Federal government is now supporting research and teaching in medicine and its related fields. A recent compilation of grants awarded by the Public Health Service for research was reported by Dr. C. J. Van Slyke, Chief Research Division of Grants and Fellowships.[6] This report lists the Public Health Service Awards made between Jan. 1, 1946 and Aug. 31, 1947, which totaled $10,214,174. Six hundred and twenty-nine scientists in 193 institutions shared in these grants which support research projects in 97 universities and colleges and in 34 hospitals and clinics.

In addition to grants for research projects, other grants are awarded by the Public Health Service for research fellowships "to encourage promising students, interested in becoming proficient in research in medical and related sciences."

As of recent date, there were 225 fellows on duty at the institutions of their choice and 131 whose term of service had not yet begun—a total of 356 fellowships, either active or pending.

Approximately $15,000,000 of Federal money are expended annually for the National Cancer Program; nearly $9,000,000 of Federal funds are available during the current fiscal year for research and training in the field of mental hygiene and psychiatry. A comparable sum is available specifically for tuberculosis. During the last session of Congress a new specialty institute was created under the National Heart Act for research and training in the field of cardiovascular diseases.

Of the funds appropriated to the Children's Bureau approximately $1,000,000 are now being spent in direct support of pediatric education.

The decision as to whether Federal support of medical education should continue, as now, in the form of short grants, largely for specific research projects or should be extended to cover a broad and continuing program with increased funds for teaching and other current expenses, is one of fundamental importance. Since it is a question which is receiving considerable attention today, any light which can be shed upon the crucial point of whether interference with university freedom has been encountered by those receiving and administering government grants becomes a matter of practical importance.

This question was the subject of an independent and direct inquiry on the part of two professors of pediatrics, both of whom have had experience with the use of Federal grants in their own departments. Dr. Myron Wegman, Professor of Pediatrics at Louisiana State University and Dr. Ralph Platou, Professor of Pediatrics at Tulane University, mailed a questionnaire to all 70 pediatric departments. They received a reply from all and report that nearly half (41%) are now receiving Federal grants either directly or through a state agency. In every instance the professors who have had Federal funds to administer indicated that there had been no interference with the use of the funds. In every instance the general experience was cited as satisfactory.[7]

In conclusion it may be said, now that the Academy's study is completed and the findings spread out before us, that one of the most important facts, though not new or unexpected, is the clear relation which is shown between services and those who are rendering the services. Better and more evenly distributed services must necessarily be predicated upon the availability of a sufficient number of physicians who, whether as general practitioners or specialists, have been well trained in the medical care and health supervision of children.

Strengthening of the teaching base therefore appears at the center of any broad program directed toward the improvement of child health. But many, if not most of the departments of pediatrics are severely handicapped by lack of funds. Lack of funds accounts for the absence of full time staff in many schools. The inability to pay part time teachers results in stringent limitation of teaching.

We are then brought face to face with the fact that the first essential in the expansion and improvement of pediatric education is an increase in the funds for current expenses for pediatric education, especially for teaching purposes.

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Panel Discussion

RHEUMATIC FEVER: SUMMARY OF PRESENT CONCEPTS

By LEE FORREST HILL, M.D., *Chairman,* JOHN P. HUBBARD, M.D., T. N. HARRIS, M.D., ROBERT L. JACKSON, M.D., GEORGE M. WHEATLEY, M.D.

INTRODUCTION

Chairman Lee Forrest Hill, M.D., Des Moines, Iowa: I should like to introduce our panel speakers. Dr. George M. Wheatley is 3rd Vice President, Metropolitan Life Insurance Company, and Chairman of the Academy's Committee on Rheumatic Fever, New York City. Next is Dr. T. N. Harris of Philadelphia. Dr. Harris is Assistant Research Professor of Pediatrics of the School of Medicine, University of Pennsylvania. He is chief of the Rheumatic Fever Clinic at the Philadelphia General Hospital. He is Assistant Consultant to the Outpatient Department of the Children's Hospital in Philadelphia.

Dr. Hubbard is Assistant Professor of Pediatrics, School of Medicine, University of Pennsylvania. Dr. Robert L. Jackson is Associate Professor of Pediatrics, School of Medicine, State University of Iowa.

MAGNITUDE OF THE PROBLEM

Dr. Wheatley.—Because of the general acceptance of rheumatic fever as a major pediatric and public health problem, we find in an increasing number of localities both the medical profession and the public ready to support organized community efforts to find cases, to provide adequate treatment, and, in fact, willing to undertake most any logical measures which promise some control over this important cause of heart disease. For intelligent planning and evaluation at the community level or on a larger scale, facts showing the magnitude and relative importance of rheumatic fever are essential.

Perhaps at this point you wonder what expressions such as "community level" and "planning and evaluation" have to do with the practicing pediatrician. As a clinician your primary concern is with the individual child. When you are at the bedside puzzled by a syndrome suggestive of rheumatic fever, it is of little help to know facts and figures on the incidence, prevalence and severity of this disease. The reason is that as a pediatrician you have a dual responsibility. As a pediatrician—especially if you are a member of the American Academy of Pediatrics—you are looked to as a leader of child health in your community. You, better than I, know how often the PTA, the Tuberculosis Association, the schools, the medical society, the health officer, and other organizations and individuals turn to the pediatrician for advice and guidance on child health matters. Because they will look to the pediatrician for help in the development of a rheumatic fever program, the data to be presented on the nationwide extent of the disease, the incidence of new cases, the trend in mortality and morbidity, and the suggestions to be offered later to improve our knowledge of these epidemologic aspects of the disease will be, I hope, not only of interest, but will lead to reasonable community efforts to combat rheumatic fever.

At the very beginning let me say that our knowledge about incidence, prevalence and severity—so important in measuring the magnitude of the disease—lacks the accuracy of data now available for many other diseases, such as tuberculosis, syphilis, or even poliomyelitis. The principal reasons for our lack of precision are, on the one hand, the absence of a diagnostic test, and on the other, ignorance, confusion, or at best, disagreement about criteria for diagnosis and recovery in either rheumatic fever or rheumatic heart disease.

Measurements of the Magnitude: Prevalence

Practically all the means of studying prevalence, such as death certificates, hospital admission records, reports of draft and insurance examinations have their limitations either from the point of view of reliability of the data or because they are not entirely representative of the general population. The house to house canvass as in a census taking, if the job is carefully done and medically

From the Annual Meeting of the American Academy of Pediatrics, Atlantic City, N.J., Nov. 21, 1948.

supervised, is perhaps the most satisfactory for information on prevalence in the general population. Such studies are rare. We have used data on heart disease obtained from the Massachusetts Chronic Disease Survey of 1929 to estimate the distribution of rheumatic heart disease in the population. In terms of the present population, there are 3 cases of rheumatic heart disease for every 1,000 persons under age 20. Between 20 and 40 years of age, the rate increases to 6.5 cases per 1,000, and reaches 8 cases per 1,000 in the 40-50 age bracket. Applying these prevalence rates nationally there are approximately 600,000 cases of rheumatic heart disease under 50 years of age.

Rheumatic Heart Disease at Ages 5 to 19

While there are undoubtedly some new cases and many more deaths from rheumatic heart disease after age 20 than before, it is of primary importance to focus on the disease in children because the peak of onset occurs during the school ages. Most of our information about its prevalence is based on studies of school populations. Many of these studies are, however, not useful for judging the magnitude of the problem in school children on a national basis. The criteria and methods used have varied with each survey. For example, some studies have selected for specialists' examination children with a rheumatic history as well as those with murmurs. Other survey reports give data for rheumatic heart disease based on the assumption that 80% of all organic heart disease recorded by school physicians is of rheumatic origin. Still other surveys have been carried out with a team of experts examining all children. Other reports are based on examination of selected grades.

School Surveys

In the following table we have selected what seemed to be the most comparable as to criteria used and number and ages examined. The rates range between 2 and 3.9 cases per 1,000 children examined between 5 and 19 years of age. It will be noted that the 4 cities selected are in approximately the same latitude.

Identified Cases of Rheumatic Heart Disease per 1,000 Children

City	Ages Included (years)	Rates per 1,000
Philadelphia 1934-36	6-18	3.9
Louisville 1936-39	6-14	3.7
San Francisco 1937-38*	6-18	2.2
Cincinnati 1936-38	5-19	2.0

Studies in rheumatic fever areas, such as Colorado and Utah, give much higher values. Wedum found a rate of 16.3 per 1,000 girls 12-19 years of age in Denver. Alway and Holley have just reported a rate of 7.0 per 1,000 among 15-18 year old high school boys and girls in Salt Lake City.

In New York City, the rate for rheumatic heart disease apparently falls in between these rates for the 2 cities in the Rocky Mountain area and the group of cities in the temperate zone. A recent report by LeLiee based on careful study of the elementary school population of about 25,000 in the Lower East Side revealed a rate of 6 per 1,000 children with definite organic heart disease of rheumatic origin.

Geographic Variation

There are few surveys made expressly to demonstrate the geographic distribution of the disease. The best known, perhaps, is the one by Paul of Indian children. He found the prevalence of rheumatic carditis among children living close to the Canadian border was almost 10 times that among children living close to the Mexican border. More recently, Sampson and his coworkers confirmed this geographic variation in a study of white school children in California. Chart 1 shows that in children living in a wet cold climate, rheumatic heart disease was six times more prevalent among children examined than those who resided in a dry warm area.

* S. J. Robinson and his coworkers have recently reported a comparable rate based on studies of San Francisco school children in 1947.

As so many of you know, this geographic factor was of considerable importance during the war. The highest attack rates of rheumatic fever occurred in those areas of the country where the mortality rates are highest.

Incidence of New Cases

We have very meager data on the number of new cases of rheumatic fever which develop each year in the general population. One of the few studies of this on a large scale has been reported recently by Collins of the Public Health Service. His data are derived from health surveys in white families in 84 cities and towns in 19 states in 1935-36. The information is limited to persons under 25 years of age. He found approximately 35 cases of rheumatic fever had developed for every 100,000 individuals under 25 years of age during the study year. In addition, 17 cases of chorea and 46 cases of heart disease were reported for each 100,000 persons under 25 years. The incidence

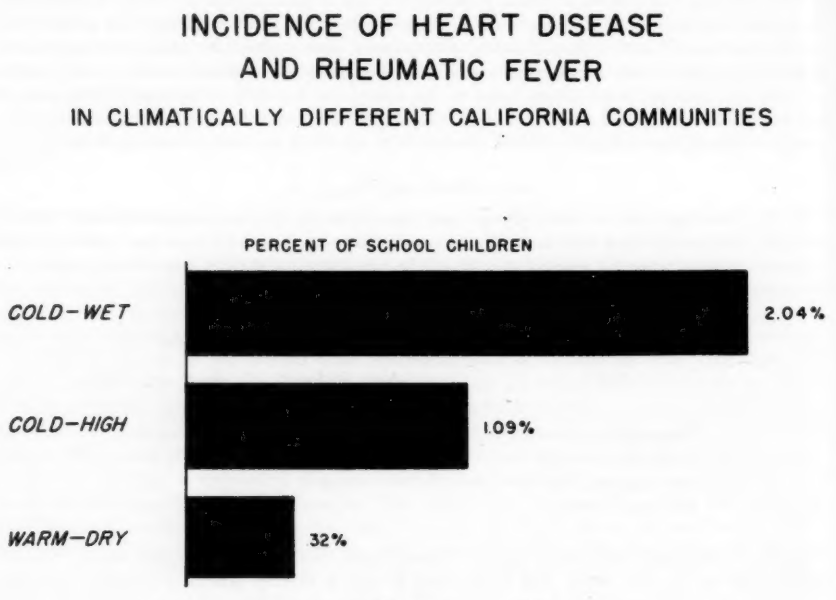

CHART 1

of new cases of all three conditions was definitely greater in large cities than in small cities and towns. The highest rates were in the West, next in the North, and lowest in the South.

Additional findings in the survey tended to confirm our knowledge on other features of the disease. For example, the disease was consistently greater in crowded than in noncrowded households. March to May was the period of highest incidence both in reported cases and deaths for the whole country, with August and September the low seasonal period for active rheumatic fever. In the study year, among rheumatic fever cases with heart complications, the fatality rate was 10.2% as compared with 1.7% among those without heart complications.

Most first attacks of rheumatic fever occur between the ages of 5 and 9. The peak of onset for both rheumatic fever and chorea lies between the ages of 5 and 14. Chorea tends to be first manifest as a rule between 10 and 14. Collins found the incidence of new cases for these conditions combined in the age band 5-14 was approximately 100 per 100,000. Using these rates, we estimate for the country as a whole the number of new cases of rheumatic fever and chorea at 5-24 ages to be about 30,000 cases per year. Included in this number are probably more than 20,000 children and young persons who develop rheumatic fever. These are believed to be minimum estimates.

Recurrences

A characteristic of rheumatic fever is its high recurrence rate. This, of course, is a very important factor not only in prognosis but in planning facilities for care. Wilson has thrown light on this subject by calculating recurrence rates in her carefully studied series of cases. She found that the individual's chance of a major recurrence was from 2 to 3 times greater in the year following an attack than after 1, 2, or more years of freedom from the disease. Age is important also. In her series, the risk of a major recurrence in patients 4 to 13 years was 1 in 4. The chance of recurrence diminished to less than 1 in 10 between the ages of 14 and 16 years. From 17 to 25 years of age, the possibility of a major recurrence was less than 1 chance in 20. Not only does this clarify our knowledge about recurrences but aids in evaluating the measures used to prevent recurrences. In view of these studies on recurrence, it would seem reasonable both in the light of our knowledge about the age of onset as well as the age when the chance of recurrence is greatest to continue to place our main emphasis on providing treatment facilities for children and adolescents.

Mortality in Young People

Mortality data are another index of the public health importance of the disease. Nearly all deaths from heart disease among persons who are 5 to 24 years of age are due to rheumatic heart disease.

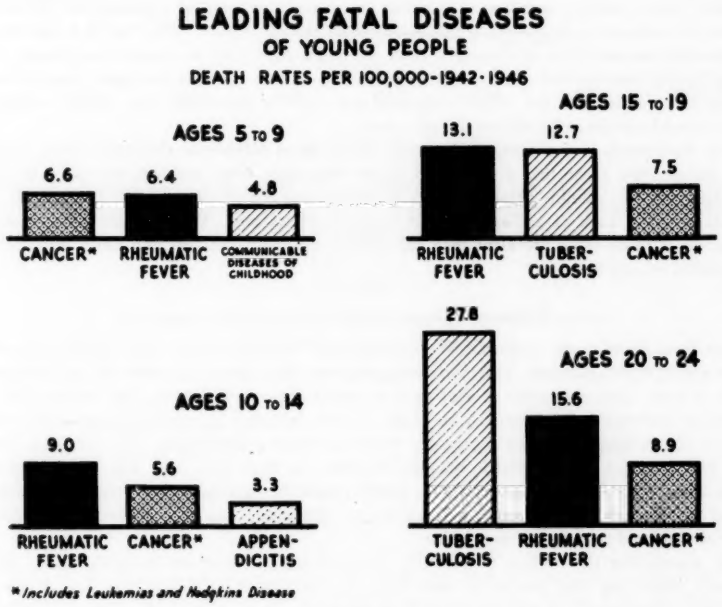

CHART 2

For this reason, the total cardiac mortality during this age period provides a minimal expression of the general mortality from rheumatic heart disease. We have recently studied the mortality among our white industrial policyholders, ages 5 to 24, for the 4 year period 1942-46, and find the following order in the leading fatal diseases at these ages (see Chart 2).

Rheumatic fever and heart disease caused more than 13% of all fatal disease in the period 1942-46 in the 5-24 age group. Chart 2 shows clearly that rheumatic fever ranks high as a cause of death throughout childhood. It is now second among diseases at ages 5-9. It will surprise most that malignancies cause more deaths than any other disease in this age group in our urban population today. At ages 10-19, rheumatic fever holds first place among the diseases and second rank at 20-24.

Disability

The magnitude of a disease, especially a chronic one, is measured less perhaps by immediate mortality than by its disabling effect. We know that rheumatic fever and rheumatic heart disease cause a tremendous amount of disability and require long and costly care. In the morbidity studies of Collins, previously mentioned, rheumatic fever patients under 25 years of age who were sick prior to the study year had an average disability of more than 6 months. The average duration in the hospital for all cases found in the survey was 51 days. More than 40% of the rheumatic fever cases were disabled 2 months or longer during the study year. Many were evidently cared for at home or had a relatively short hospital stay because only 30% of the cases went to a hospital at any time during the study year and less than 8% of those confined to bed were in a hospital 2 months or more during that year. Fifty-nine per cent of those incapacitated by rheumatic fever were cared for by private physicians who averaged nearly 13 visits, most of them house calls during the study year. More than a fifth of the rheumatic fever cases who had home calls had 20 or more such calls. In slightly more than 10% of the cases, a visiting nurse was used, and practically none had a private duty nurse.

When one considers that this is only a partial picture of the care received or required by this group of new cases of the disease; that the likelihood of recurrence is greatest for the group as a whole in the year following; and that many individual members of the group will continue to require treatment for years to come, one begins to visualize the enormous amount of treatment and the cost necessary for the adequate management of this or any other chronic disease. What would it cost to provide care for only the new cases of rheumatic fever we might expect for the country as a whole? Assuming the cost of hospital and medical care at $10 a day—a very conservative figure today—to provide 50 days care for each of the 20,000 estimated new cases of rheumatic fever in the 5-24 year old group—would amount to 10 million dollars a year.

How widespread is the disease? We have talked about full-blown rheumatic fever, chorea and heart disease. We know that a large part of the rheumatic fever problem, especially in terms of early diagnosis and possible prevention, lies in determining the presence of the disease at the earliest possible moment. Lack of a diagnostic test hampers efforts now. Yet there are some who believe the disease is much more prevalent than our school case-finding surveys and death certificate, clinic and hospital studies indicate.

Evidence of Decreasing Mortality and Morbidity

Even from these crude measures, the magnitude of this disease is clear. Rheumatic fever is a serious public health problem. There are some observers who think it is definitely less prevalent and milder in form. This experience is supported by data from several sources. One evidence for this is the steady downward trend over many years of the mortality in young people (see Chart 3). Actually, the decline since 1920 among our white industrial policyholders (5 to 24 years) has been about 80%. Within the last decade the rate has been cut more than half. The number represented in this insured age group 5-24 over this whole period has averaged more than 6 millions. The method of selection of the insured has not varied. The group can be considered representative of the urban child and young adult population.

The reasons for the decline in mortality from rheumatic fever are probably many. But it is extremely interesting and worthy of note that the mortality from this disease has shown such a remarkable improvement in spite of our lack of knowledge as to its etiology and cure. Factors which undoubtedly contribute to this decline are the general improvement in child health care with its elements of improved nutrition, protection from communicable diseases and better treatment of acute illnesses. On this latter point, it is worth observing the pace at which the mortality rate was declining has accelerated since chemotherapy was introduced in the treatment of streptococcal and other infections. Thus, the mortality in children both white and colored ages 5-14 insured in our industrial department declined only 22% in the 7 years prior to 1940 in contrast to a decline of 65% in the comparable period after 1940. The same trend in mortality in young people has been observed in Great Britain.

The incidence of cardiovascular defects among draftees in World War I and World War II suggests that there may be less organic and therefore less rheumatic heart disease today. Table I compares those cardiovascular defects most likely to be of rheumatic origin. The rate for valvular

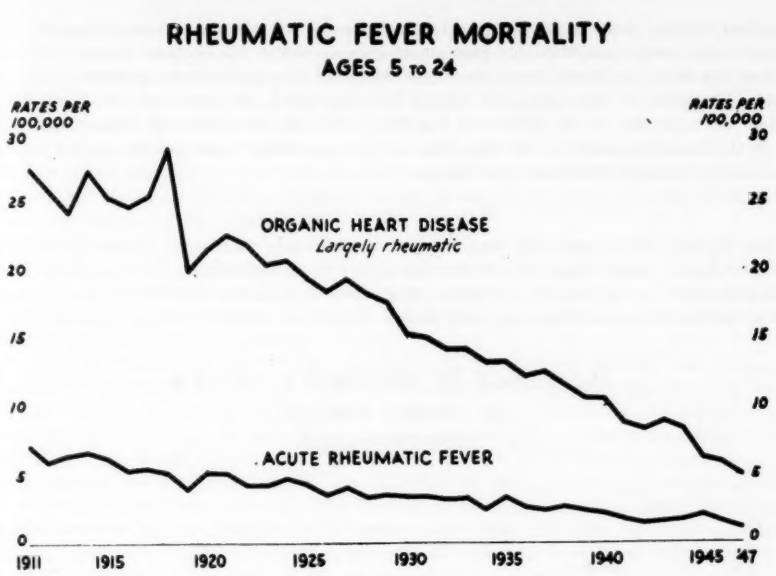

CHART 3

heart disease in young men in World War I was about twice the rate of those examined in World War II. The limitations of this data are appreciated. On the other hand, they seem reasonable in the light of the facts on the mortality trend in the period between the two wars.

TABLE I

Incidence of Cardiovascular Defects per 1,000 Men Examined
U. S. Selectees World War I and II

	Valvular heart disease	*Cardiac hypertrophy*
World War I (age 21-31)	29.6	4.4
World War II	16.5*	1.8
World War II (age 18-19)	15.9*	0.9

* Includes rheumatic heart disease.

A study of the trend in incidence of cases of rheumatic fever in the armed forces from 1900 to 1945 shows a much faster relative decrease in the incidence of rheumatic fever between the two world wars than was true of mortality in the general population of all ages. During World War II, in spite of the large number of cases of rheumatic fever in the armed forces, the rates were only about a tenth of those prevailing during World War I. The large number of cases, about 40,000, is accounted for by the much greater number of individuals in service as well as the greater length of World War II (Chart 4).

The gist then of this statistical review of the magnitude of rheumatic fever is that we have probably somewhere in the neighborhood of 600,000 individuals under 50 with hearts damaged as a result of the disease. Every year at least 30,000 new cases of rheumatic fever and chorea develop between the ages of 5 and 24. There is considerable geographic variation in the prevalence of the disease as judged by surveys among school children in various parts of the country. Rheumatic fever and heart disease cause more deaths at 10-19 than any other disease. It is undoubtedly the most

important chronic disease in this age group with the cost of care running to many millions of dollars annually. For many years, there has been steady improvement in the mortality at ages 5-24 with a marked downward acceleration noted since 1940. Morbidity also appears to be declining.

The limitations of these data have already been mentioned. We have sufficient information to outline the magnitude of the disease on a national scale. But we need more accurate information on local prevalence, incidence of new cases and severity before there can be much progress in establishing community rheumatic fever programs.

Ways to Increase Precision

The first step toward improving the accuracy of our knowledge is better recognition of the disease. Until we have a simple diagnostic test, we will always be in doubt about many cases both of acute rheumatic fever and rheumatic heart disease. Meanwhile to make our case-finding more certain, we should develop rheumatic fever and heart disease consultation service for young people. This can

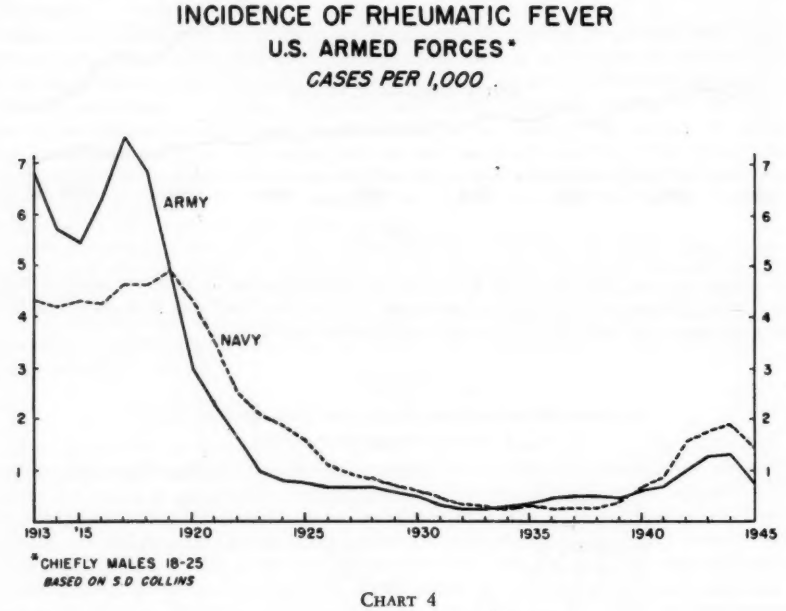

CHART 4

be either as an adjunct to the school medical examination program or as a community service provided by the health department of a voluntary agency such as the local tuberculosis or heart association. From the point of view of sound public health practice, when the community has a good health department, the service should be developed by the official agency and be accepted by the local medical profession.

Experience with diagnostic services shows that of those cases sent to an experienced physician for review, in one third of the cases, he is unable on the first visit to decide about the diagnosis. This in no way minimizes the value of this consultation service. It only emphasizes the difficulty of diagnosis. It is a necessary, though expensive, part of a rheumatic fever program at this stage of our knowledge about case-finding. This service is valuable economically because it saves expense of treating well children and psychologically because it prevents some children from developing an invalid complex.

A second and urgent need is agreement by rheumatic fever authorities on diagnostic criteria. Following this there should be widespread adoption of this common language. From our study of

survey data, as previously described, few observers use the same criteria in identifying either rheumatic fever or rheumatic heart disease. This was recently re-emphasized by Alway who pointed out that his statistics were not comparable to those of Wedum because of differences in criteria, chiefly in the diagnosis of mitral insufficiency. She made no mention of the intensity of the murmur nor of its marked alteration by respiration or change of position.

Until we get some degree of uniformity, we will be unable to have accurate knowledge on national prevalence. Such guides for diagnosis would also be of great aid to the school physician and the practicing physician. Teaching of criteria would be logical and prime objective in rheumatic fever postgraduate education programs.

The third essential step toward improving the reliability of our data is in the field of medical education. The practicing physician must have more opportunity to learn about the disease. The development of consultation service provides a logical clinical teaching facility. Pediatricians and cardiologists should work together to establish postgraduate teaching in this field through county medical societies especially in rural areas.

Making the disease reportable is advocated as another method to determine the size of the rheumatic fever problem in a locality. Successful reporting of a disease assumes that it is readily recognized by the vast majority of physicians. Moreover, public health officers find that the most completely reported diseases are those which on being reported lead to a service for the patient. For example, in a case of tuberculosis, notification generally leads to follow-up by the health department and arrangement, frequently, for sanitorial care. When typing service and type serum were made available in the treatment of lobar pneumonia, the reporting of the disease improved rapidly in areas where health departments offered serum and other services to reporting physicians. Since the use of sulfa drugs and penicillin, health officials have observed pneumonia case reporting to have fallen off out of all proportion to the drop in the mortality. Rheumatic fever has been made a reportable disease as a first step in a rheumatic fever program in a number of states and cities, but I know of no place where the procedure is more than a gesture. An intensive educational program with the medical profession in the locality is necessary to good reporting. In addition, special services, such as consultation, hospital or convalescent home nursing care, or special home teaching should be available as services to offer to the physician for the care of his patient. Until such a program, or elements of it at least, has been developed, I believe it is inadvisable to make the disease legally reportable. When such services can be offered a practical way to put these facilities on an operating basis is to establish reporting.

And finally, the development of a rheumatic fever register is suggested as a means of refining our knowledge as well as aid in the managing of the disease. The purpose of a register is to implement with specific mechanical procedures the program of service to rheumatic patients. It requires a central clearing house in the community where a record is kept of every individual in that locality who has had an attack of rheumatic fever or who has rheumatic heart disease. The purpose of such a file is to have not only a complete picture of the magnitude of the rheumatic fever problem in the area but to help provide and to maintain the continuity of medical care. A very successful register for cancer control has been in operation for many years in Connecticut. Much valuable information on prognosis has been obtained.

As in the case of making rheumatic fever a reportable disease, before a register can come into being, several other steps are necessary. The first and most logical is to survey all community resources. Existing facilities should be studied for inadequacies, unnecessary overlapping and duplication. With this comprehensive knowledge, a program can be planned to utilize fully existing facilities and to secure necessary supplemental services.

Then, before a useful register can be created, there must be agreement by the medical profession and all agencies rendering direct service to the rheumatic to centralize responsibility for integration of the various services which each provides. There must be agreement, too, on what constitutes adequate service. Such criteria have been set up for cardiac clinics, but there should be similar guides for appraising the quality and adequacy of all services and facilities. There should also be minimum standards for the frequency and kind of care and follow-up required by each type of patient to be included in the program.

At the present time, there is no place in the United States where these conditions prevail. Efforts are being made in several places—for example, Los Angeles, New Haven, and the Lower East Side of New York City—to develop a register and study its operation. A register is a logical and essential

part of a community rheumatic fever program but until we have a body of knowledge based on field study, it cannot be recommended as a practical procedure for immediate adoption by communities.

In conclusion, one measure of the magnitude is our estimate that about 600,000 persons under 50 years of age have rheumatic heart disease. Approximately 30,000 cases of rheumatic fever and chorea develop yearly in the ages 5-24. In temperate zones about 3 cases per 1,000 children in the school age group have rheumatic heart disease. In more severe climates, rates of 7 and even 16 per 1,000 children have been reported. On the other hand, mortality has been decreasing steadily for the past 20 years. In the past 7 years, the decrease has been 3 times faster than for the preceeding 7 years.

Five points were suggested to clarify and further refine our knowledge about the magnitude of rheumatic fever in this country. The first, adoption and promotion of diagnostic criteria, is recommended for immediate action by the Academy of Pediatric's Committee on Rheumatic Fever. Two others can be put into action almost at once in any locality where there is a local support and readiness for action. They are (1) a community consultation service and (2) a postgraduate medical education program.

The last two, reporting the disease and development of a case register, depend upon the development and coordination of facilities for the diagnosis and care of the disease. They can only come about after considerable time and cooperation by the various community groups who are concerned. Introduction and acceptance of the first 3 steps should better pave the way for the last 2 suggestions.

In addition to furnishing more reliable data upon which to judge the effectiveness of control efforts, we believe these 5 recommendations will result in better care of rheumatic fever.

These are not new or revolutionary ideas in medicine or public health. Very much the same approach has been employed to improve our knowledge and the care of tuberculosis. Pediatricians as child health leaders of the community can and should take an active part in developing these activities.

Etiologic and Diagnostic Considerations in Rheumatic Fever

Dr. Harris.—The etiology of rheumatic fever is today unknown, despite the large volume of work which has been done on the cause of this important disease, and despite a number of suggestions which have been offered as to possible causes. In the absence of a known etiology, we do not have available a specific diagnostic test or specific prophylaxis and therapy. This review will discuss what has been done along the chief lines of investigation of the etiology of rheumatic fever, and the application of these researches to the problem of laboratory diagnosis of the disease. Many workers have called attention to the importance of predisposing factors of heredity and nutrition in the etiology of rheumatic fever. In this paper these aspects will not be discussed.

The chief currents of investigation in etiology have arisen from those facts in the natural history of the disease which could serve as starting points for such investigations. First, the only observations which point to any known agent as a possible cause are those relating to Str. hemolyticus. Second, rheumatic fever is an infectious disease for which no infecting bacterium has been identified. It has therefore been suspected that a filterable virus might be the cause of the disease, and attempts have been made to identify such an agent. Third and finally, the pathologic picture has struck many workers as being so similar to that found in states of hypersensitivity as to suggest a number of possible theories of etiology. Because of other evidence linking Str. hemolyticus to rheumatic fever, some workers have felt that patients may be hypersensitive to some product of Str. hemolyticus or to some part of the organism itself. There is, however, no experimental evidence for this at present. Another possibility is that rheumatic fever is caused by hypersensitivity to some antigen of the host tissue which has been altered by a pathologic effect of Str. hemolyticus. It has been postulated that new antigens can be formed by the conjugation of human proteins and streptococcal substances. Such conjugated antigens have in turn been thought to give rise in the rheumatic subject to "auto-antibodies" to human cardiac tissue.

A. Rheumatic Fever and Str. Hemolyticus

The data which suggest a relation of the Str. hemolyticus to rheumatic fever can be divided into three parts: first, the epidemiologic evidence; second, serologic data, involving almost entirely the antistreptolysin and antifibrinolysin tests, which were recorded before the war; and, third, other and more recent serologic work.

(1) *Epidemiologic Data:* Epidemiologic studies have pointed in a number of ways to some connection between streptococcal infection and rheumatic fever. The similarity in geographic distribution of streptococcal pharyngitis and rheumatic fever is suggestive; the seasonal occurrence of streptococcal upper respiratory infections and rheumatic fever is closely parallel, and during those years in which the incidence of streptococcal upper respiratory infections is high the incidence of rheumatic fever is high. It has also been reported that whereas in the population at large approximately 5% of patients with streptococcal pharyngitis may contract rheumatic fever later, this percentage may be as high as, or higher than, 50% among quiescent rheumatic patients. Similarly, among families which have a high incidence of rheumatic fever, the rate of occurrence of rheumatic reactivations is further increased following epidemics of streptococcal pharyngitis which involve those families. Even more striking than these observations, however, are the studies which have shown repeatedly that cases of rheumatic fever often follow known acute streptococcal upper respiratory infection by an interval usually varying between 10 and 20 days. More data on this relationship have been obtained in institutional groups, including military barracks. In such groups, epidemics of streptococcal infection have frequently been followed by waves of rheumatic infections or reactivations, involving a considerably smaller number of subjects, the majority of whom were convalescents from the foregoing streptococcal infections. This body of data has been comprehensively reviewed by Paul, and will not be discussed further here.

(2) *Antistreptolysin and Antifibrinolysin Studies:* The suggestion implicit in the above data, that Str. hemolyticus might have a special role in rheumatic fever, gave rise to a large volume of serologic investigation of the subject in the decade following 1932. Some of these studies employed reactions technically unsuited to quantitative estimation, such as agglutination of Str. hemolyticus and various precipitin tests. The great majority of this work, however, involved the measurements of neutralizing serum antibodies to two biologically active substances liberated by Str. hemolyticus into its culture medium, namely, the hemolysin and fibrinolysin. These neutralizing antibodies were found by many observers to be elevated above the normal range in active rheumatic fever, as was the case in convalescence from acute streptococcal infection. In the more extensive and careful studies of this subject it was found, however, that not all patients with active rheumatic infection showed such elevated titers, and that approximately only three-quarters of the patients studied during a reactivation of the rheumatic process showed a definite increase in the antistreptolysin titer at the time of the reactivation. This work involved, in the main, a single serologic reaction in the case of but 2 of the many antigenic entities involved in the contents and products of Str. hemolyticus, and thus tested only a minute part of the possible area of contact between that organism and the tissues of the rheumatic host. Nevertheless, some of the authors of the studies involved ventured to draw broad conclusions from their data as to whether any relation existed between the streptococcus and rheumatic fever. These conclusions ranged from one extreme, in which the data were interpreted as proving that Str. hemolyticus is the cause of rheumatic fever, to the opposite extreme, i.e., that the data proved that this organism had no relation to the disease.

It has been shown that climatic and epidemiologic factors caused a rather wide variation in the range of titers found in normal, post-streptococcal and active rheumatic groups, respectively, from series to series, but that within each series the rate of elevated titers, and their range, was quite similar in the post-streptococcal and rheumatic groups. This similarity in range of titers in the two clinical groups made, in essence, an immunologic diagnosis of foregoing streptococcal infection in patients with active rheumatic fever, thus supporting the epidemiologic evidence for a relationship between the two. It was pointed out that this suggestion of relationship of rheumatic fever with Str. hemolyticus as an etiologic organism was not in conflict with the failure of these data to identify the hemolysin or fibrinolysin as a means by which that organism might cause the changes in rheumatic disease. No investigation, no matter how thorough, of the effect of contact between the tissues of the rheumatic host on one hand, and only two antigens of Str. hemolyticus on the other, could be said to rule out the streptococcus as an etiologic agent, and, conversely, only by the most unusual good fortune could these investigations have chanced on a pathogenetic mechanism in one of the two antigens studied.

A definite study of the etiology of rheumatic fever in relation to Str. hemolyticus should, of necessity, be much wider in its scope, even within the immunologic field alone, aside from the other possible mechanisms by which a microorganism can cause disease. Within the field of immunologic

reactions, for example, a conclusive study of such a possible relation would necessarily include an examination of tissue sensitization and humoral antibody concentration in rheumatic fever to every immunologically distinct antigen in the streptococcal cell and among its products in culture, regardless of the significance of these substances in terms of toxic or other biologic effects, of virulence or of antigenic classification.

(3) *Recent Studies in the Streptococcal-Rheumatic Fever Relationship:* Recent studies in the etiology of rheumatic fever have, in fact, taken cognizance of the broad area of possible contact with the streptococcus. Reports of an investigation of the etiology of rheumatic fever in progress in these laboratories have described the fractionation of the entire streptococcal cell by disruption of the organism and differential centrifugation. Antibodies to two of these fractions have been measured in the sera of patients with streptococcal and rheumatic infection, with results rather similar to those of antistreptolysin tests, i.e., titers elevated above the normal range in a considerable majority of patients with active rheumatic fever and after streptococcal infection, with similarity in frequency and range of elevated titer in the two groups of patients. It was concluded that these serologic data, again, supported the concept of a relationship of rheumatic fever to Str. hemolyticus as an organism, without implicating these two antigens in particular.

Work has also been reported from these laboratories and others on measurements of neutralizing antibodies to streptococcal hyaluronidase, an enzyme produced by Str. hemolyticus and by some other bacteria which digests hyaluronic acid. (The latter is a chief constituent of hyalin, which is the matrix of hyalin connective tissue.) Friou and Wenner derived indices of neutralization of the enzyme for sera of patients with streptococcal and rheumatic infection, and found amounts of the antienzyme to be increased in both groups of patients, with no significant difference between the groups. In a study of sera of rheumatic patients, Quinn found that the mean titer of a group of active rheumatic patients against streptococcal hyaluronidase was significantly higher than that of a comparable group of early post-streptococcal convalescents.

Work on streptococcal hyaluronidase in rheumatic fever has been carried on in our laboratories, simultaneously with the work just reported. In a first study, we tested the effect of this enzyme in enhancing the spread of indicator dyes in the skin, and found no greater spread of dye in the skin of patients with rheumatic fever than in normal subjects, in contrast to the results reported by Guerra. The greater part of our work with streptococcal hyaluronidase consisted of verifying the validity and specificity of a serologic test for antibodies to this enzyme, and applying this test to measurements of such antibodies in the sera of several groups of patients. It was found that the antihyaluronidase titer, as measured by the mucin-clot-prevention test, was elevated in both streptococcal and rheumatic disease, as was true of the antistreptolysin and of the antibodies to the two streptococcal nucleoprotein fractions developed in these laboratories which were referred to above. However, whereas the mean titer in active rheumatic fever was slightly (less than 2-fold) higher than that following streptococcal infection in the case of the other 3 antibodies, it was found to be 8- to 10-fold higher in the case of antihyaluronidase. This difference can be seen in Fig. 1. The percentage frequency for each titer in each group of patients tested is outlined in the figure. The geometric mean titer, indicated by the broken line, is 580 for the group of active rheumatic patients, and 73 for the group of post-streptococcal convalescents.

In further comparison of the antihyaluronidase titers with those of the other 3 antibodies, it was shown that the antihyaluronidase titer was better correlated with changes in the state of activity of the rheumatic process than were the others. This was demonstrated by comparative time-graphs of the respective titers with those showing the clinical severity of the disease, by comparison of time of return of the titers to their respective normal levels in relation to clinical quiescence of an acute episode of rheumatic fever, and finally, by greater and more constant rise of antihyaluronidase titer at a time of clinical reactivation of the disease. This last point was one of some importance for the streptococal theory of rheumatic fever, for although the antistreptolysin titer failed to rise in 23% of the reactivations of the infection (the percentage was somewhat higher in the case of the other 2 antibodies), the antihyaluronidase titer rose in each of the 22 reactivations studied. (In the case of the antistreptolysin, this percentage agrees with that reported in the earlier literature, where the failure of this antibody to rise at every rheumatic reactivation was presented as a paradox for the streptococcal theory of the etiology of this disease.) These differences are shown in Table I.

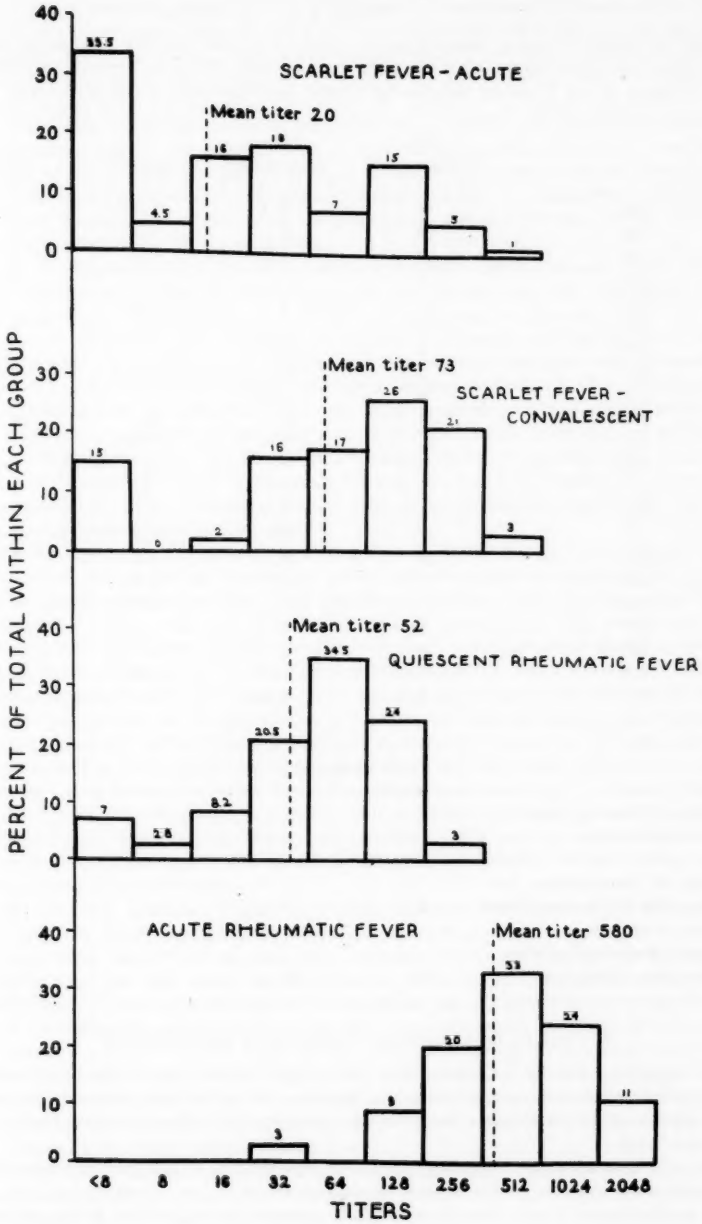
SCARLET FEVER - ACUTE
Mean titer 20
SCARLET FEVER - CONVALESCENT
Mean titer 73
QUIESCENT RHEUMATIC FEVER
Mean titer 52
ACUTE RHEUMATIC FEVER
Mean titer 580
PERCENT OF TOTAL WITHIN EACH GROUP
TITERS
<8
8
16
32
64
128
256
512
1024
2048

FIG. 1

TABLE I

INCREASES IN TITERS TO THE 4 STREPTOCOCCAL ANTIGENS IN THE SERA OF RHEUMATIC SUBJECTS AT THE TIME OF RECRUDESCENCE OF RHEUMATIC ACTIVITY: RATIO OF TITERS IN ACTIVE DISEASE TO THE TITER OF THE PATIENT DURING THE PRECEDING QUIESCENT PERIOD

		Anti-hyaluronidase	Anti-streptolysin	Anti-CP	Anti-S
	RB	4	1.4	1.4	—
	EB	16	32	—	2
	AB	32	1.4	—	2
	RB	8	2	—	2
	CB	16	2	1.4	—
	FC	4	2	4	4
	GD	8	2.8	—	—
	GE	2.8	4	1.4	1.4
	LF	4	1.4	—	2.8
	JF	24	32	4	4
	KF	12	5.6	—	2
	MH	5.6	—	—	2.8
	JI	11.2	—	—	4
	TJ	2.8	1.4	2	1.4
	LJ	32	2	2.8	2
	WL	45	2.8	1.4	4
	LM	2.8	—	1.4	—
	FM	8	—	2.8	—
	JP	8	2	—	—
	BP	8	2	—	—
	EP	5.6	—	1.4	2.8
	DS	8	1.4	2	2.8
Total	22				
		— = no change			
Mean Ratio of Titers at Height of Episode to that before		8.80	2.46	1.60	1.88
Percentage of Reactivations for Which no Rise in Titer was Found		0	22.7	41	32
Percentage of Reactivations Showing Less than a 2-fold Rise		0	45	73	41

B. Virologic Investigations of the Etiology of Rheumatic Fever

In the intensive search for a microorganism which might be the cause of rheumatic fever, there were scattered investigations over the years for a possible viral agent. Since these are less accessible than the studies on Str. hemolyticus and rheumatic fever, we shall attempt to cover them in somewhat greater detail.

In the early decades of the 20 century, De Vecchi reported that he had produced myocarditis in various laboratory animals by the injection of bacteria-free blood of rheumatic patients. Natali reported similar results 9 years later. In a carefully controlled study in 1924, Miller attempted to transmit rheumatic fever to rabbits and guinea pigs by the injection of tissues and fluids from rheumatic patients. A series of 67 inoculations and passages in rabbits produced 2 cases of out-spoken arthritis. In about ½ of the rabbits and ⅔ of the guinea pigs microscopic lesions were encountered in the myocardium, consisting largely of interstitial accumulations of lymphocytes and endothelial

cells. What is most valuable, perhaps, for our understanding of data which have accumulated through the years, is that in the same laboratory over a period of a few years more than 60% of presumably normal rabbits showed, at autopsy, myocardial lesions consisting of accumulations of lymphocytes and endothelial cells in varying proportions. In view of the latter finding, Miller concluded that his attempts to pass a virus of rheumatic fever were unsuccessful. It is well to remember the occurrence of microscopic myocardial lesions in presumably normal rabbits, in attempting to understand other work. Gross, Loewe, and Eliasoph later reported an unsuccessful attempt to infect various animals with blood, exudates and filtrates of tissue emulsions from active rheumatic fever patients. Wilson, in 1934, also attempted, with no apparent success, to infect two chimpanzees with materials from rheumatic patients. The animals were observed over a period of 3 years, and no evidence of the transmission of rheumatic fever was obtained.

Brokman, in Poland, in 1935, reported a complement fixation test for rheumatic fever, using as antigen a homogenate of livers of rheumatic patients. During the same year, Schlesinger and his group in England reported the results of a search for a viral agent in rheumatic fever. High speed centrifugation of pericardial fluid withdrawn at autopsies of rheumatic subjects yielded a small deposit. This material was washed by centrifugation and resuspended. Microscopic examination showed, in addition to fragments of cellular protoplasm, small particles of uniform size, resembling elementary bodies as found in many viral diseases. This was highly suggestive, and the authors proceeded to perform microscopic agglutination tests with sera of active rheumatic fever patients and the suspensions of "elementary bodies." Of the sera of 8 patients with active rheumatic fever, 7 caused the suspensions of "elementary bodies" to flocculate, whereas the sera of non-rheumatic patients failed to do so. In addition, similar suspensions derived from pericardial fluid of patients with other infections were not agglutinated by rheumatic sera.

Eagles and his group in England were able to confirm the earlier findings of Schlesinger. Following similar procedures, they found "elementary bodies" and were able to cause microscopic agglutination of these bodies with rheumatic sera. They also observed serologic cross reaction among rheumatic fever, rheumatoid arthritis, and chorea. In further studies on the subject, they attempted to infect monkeys with the "elementary bodies" they had obtained from pericardial fluids of rheumatic patients, but were unable to do so. Schlesinger et al. attempted to infect a variety of laboratory animals with preparations of "elementary bodies," but were also unsuccessful. The war put an end, for the most part, to this line of investigation in England. At about that time an investigation was undertaken by Hubbard (at the House of the Good Samaritan in Boston) in which a great variety of animals, as well as embryonated hens' eggs, were injected by many routes, with materials obtained from patients known to have rheumatic fever. No evidence was obtained in this extensive search to indicate possible transmission of rheumatic fever. Further attempts to isolate "virus-like" bodies from fluids obtained from patients with rheumatic fever and to detect antibody to these bodies by the agglutination, complement-fixation and precipitin tests failed to corroborate the findings reported earlier by the other workers mentioned.

Copeman, in 1944, inoculated a group of human volunteers with blood drawn from an adult with acute arthritis, involving stiffness of joints, and a faint mitral systolic murmur. The experimental subjects experienced slight fever and limb pains, and when blood was passed from them to other volunteers, some of the latter group had muscle pains. After the 4th passage, the effect was lost.

MacNeal and his group reported that they were able to pass an agent from the blood of a child acutely ill with rheumatic fever into chick embryos. Embryonic tissues and fluids of infected eggs were collected and passed to other eggs and to rabbits. Neither eggs nor animals receiving the material died or showed any gross pathologic lesions, but microscopic lesions were reported which the authors interpreted as evidence of successful passage of the viral agent of rheumatic fever. Without any available data on analogous experiments with control materials, and without any serologic data, it is difficult to give much credence to this work.

As the work on a viral etiology of rheumatic fever is surveyed, it becomes clear that a number of observations have been made which cannot be fully evaluated. The serologic data accompanying much of the work is not adequate. On the other hand, the failure of various investigators to transmit to laboratory animals a disease process similar to rheumatic fever does not preclude the possibility that the materials used contained an active agent. It must be borne in mind that if there is a viral agent involved in the etiology of rheumatic fever, it may not show the same type of relationship to the disease process as we find generally between bacterium and host. The absence of direct contagion

in the epidemiology of rheumatic fever, and the overwhelming amount of evidence linking Str. hemolyticus to this disease seem to point to the possibility of some unusual type of relation of organism and host tissue. With the increased knowledge in virology and its technics, as well as the increased knowledge gained over the years regarding Str. hemolyticus, it is necessary to open once more the question of viral etiology, perhaps in some relationship with Str. hemolyticus.

C. Investigation of Auto-Antibodies

The fact that the living animal does not, under normal circumstances, develop antibodies to tissue proteins of its own species is well known. Various workers have produced serum containing antibodies to kidney or other tissues by injecting extracts of the kidney of an animal into an animal of another species. When that serum was introduced into the animal against whose kidney tissue the antibodies were produced, characteristic lesions were found in the kidneys of the injected animal. This was taken to indicate that pathologic lesions can be caused by the presence of antibodies to the native tissue. Further work demonstrated that it was possible to cause an animal to produce antibodies to organs of his own species under special circumstances. Thus, Burky injected into rabbits toxic filtrates of staphylococcus which had grown on broth prepared from lens substance. He then found that these rabbits became sensitive to plain lens substance, as judged by the skin test. Analogous auto-sensitization to rabbit muscle tissue was produced by using toxic filtrates of the same organism grown in a medium containing rabbit muscle. Schwentker and Comploier obtained complement-fixing antibodies to rabbit kidney following the injection of rabbit kidney together with staphyolocal toxin. Cavelti later showed, by use of the collodion particle technic, that rabbits and rats injected with homologous kidney substance plus streptococcal substances developed antibodies to plain kidney of their own species. In rats it was found that as a result of this procedure, inflammatory lesions resembling those of glomerulonephritis were produced in the animal. In an attempt to apply the same type of study to rheumatic fever, Cavelti found that rats injected with streptococci plus extracts of rat heart, rat skeletal muscle, and rat connective tissue, developed antibodies to the respective tissues, as measured by the collodion particle technic. The rats also showed certain microscopic changes affecting chiefly the valves and the other connective tissue structures of the heart. These changes were described as resembling, in a broad sense, those of rheumatic fever. In further studies of rats focally infected with Str. hemolyticus group A autogenous tissue antigens appeared to be released into the blood stream during the height of infection, and subsequently auto-antibodies to rat tissue were found. The auto-antibodies described were not highly specific, as might be expected, since the type of tissue injected was not pure muscle or pure connective tissue, free of contamination with the other type. In addition, it was found that measurements of the auto-antibodies had to be made generally within 24 hours of collection of the serum, as the measurable amount of auto-antibody seemed to decrease rapidly on storage. In an effort to apply this work to the problem of rheumatic fever it was found, of 67 sera of rheumatic patients, the majority reacted positively in the collodion particle test to an antigen prepared from a presumably normal heart, indicating that these sera contained antibodies to that tissue.

The significance that such findings might have for rheumatic fever is obvious. However, a number of questions arise in considering the studies. It would certainly be desirable to be able to demonstrate the auto-antibodies by immunologic technics other than that of the collodion particle method. This latter method is easily disturbed by physicochemical factors, and is often difficult to interpret. (An antibody demonstrable by one serologic technic should be demonstrable by some other as well.) Some speculation arises also because of the lability of the auto-antibody described. In general, most antibodies are quite stable, although under certain circumstances antibodies are encountered which are found to deteriorate upon prolonged storage in a non-frozen state. The fact that it was necessary to measure these auto-antibodies within 24 hours of collection of the serum raises the question of what exactly was measured, whether it was true antibody, and, if so, of what kind.

The fact that the reaction of tissue antigens with homologous auto-antibodies seems to lead to pathologic lesions which "in a broad sense . . . may be considered to resemble those of rheumatic fever" cannot in itself bear the brunt of the evidence, since many types of proliferative inflammatory lesions of a microscopic scale in experimental or even in normal animals may, to that extent, resemble those of rheumatic fever.

Although the studies referred to have been reviewed with some evaluation of their methods and

results, it would be ill-advised, and, by any proper standards, impossible, for this review to attempt judgment as to which of the three agents discussed might most likely be the cause of rheumatic fever.

Diagnostic Considerations

The great mass of experimental work on the etiology of rheumatic fever has yielded very little data which might be applied to the problem of the laboratory diagnosis of active rheumatic fever, and none at all for such diagnosis of the quiescent state of the disease.

The work on possible viral agents and on auto-antibodies has, of course, no application to this problem in their present state of development. The streptococcal data must be considered in two parts: the older work on antistreptolysin titers, and the more recent work with antihyaluronidase.

The work with antistreptolysin had little to offer in the way of diagnostic application. As has been pointed out, the titers of this antibody in active rheumatic fever, although elevated for the most part, were not, as a group, higher in that state than following streptococcal infection. Since, moreover, it was shown, especially by Mote and Jones, that the antistreptolysin titer frequently remains elevated for many months after a streptococcal infection, an elevated antistreptolysin titer in a patient suspected of having active rheumatic fever could only be interpreted as implying that diagnosis with the proviso that the patient had had no streptococcal infection for many months prior to the time of examination. The severe limitations thus placed on this test as a diagnostic tool for rheumatic fever are obvious.

In the case of the antihyaluronidase test, however, a number of the titers found among the cases of definite rheumatic carditis studied thus far were above the upper limit of the titers observed after streptococcal infection. (In this series of 126 patients with active rheumatic fever, 55, or 43%, showed such higher titers.) Since these titers were also well above the range found in the normal population it was possible to interpret the antihyaluronidase tests of these 55 patients as suggesting active rheumatic infection. This work is, of course, in an early stage; in a quantitative sense, it may well be that the percentage of antihyaluronidase titers in active rheumatic fever which lie above the "post-streptococcal" range will differ in other places and in other years from that observed by us thus far. It is, however, encouraging to note that a diagnostic procedure may now exist by which active rheumatic infection (not necessarily in its most severe form) can be diagnosed in at least ⅓ of the cases, and by which reactivations of rheumatic infections in the quiescent subject can be diagnosed in all or almost all cases, provided that appropriate serum specimens are available.

WHEN DOES AND WHEN DOESN'T A CHILD HAVE RHEUMATIC FEVER?

Dr. Hubbard.—During the course of physical examination of school children in one of the large cities of the East, close to 3,600 children were listed in a so-called "cardiac record" because school physicians and nurses found symptoms or signs considered to be indicative of rheumatic fever or heart disease. Upon closer examination only 22% of these were diagnosed as having organic heart disease. One would like to know how long it took to remove from the mind of parent, teacher and child all apprehension arising from the fact of having been, even though temporarily, listed in a "cardiac record."

This situation, which could be repeated in many places throughout the United States, is cited to demonstrate both the difficulties and importance of accuracy in the diagnosis of rheumatic fever and rheumatic heart disease. In this disease we are confronted with many strange paradoxes. It kills more children and cripples them more often than any other disease, but it has received little attention in comparison to its seriousness. It is admittedly one of the most widespread diseases of childhood, yet pediatricians have shown less interest in it than cardiologists. It occurs in epidemic form, yet it is not generally reportable. Despite its prevalence and severity its cause is unknown, its diagnosis difficult. There is probably no other common ailment of man that is misdiagnosed as often as rheumatic fever. Because of a functional cardiac murmur of no consequence, a child may be withheld from athletics or even confined to bed for long periods of time. On the other hand, because parent, teacher or physician is unaware of the early symptoms of rheumatic fever a child with active infection may be allowed full and continued activity.

Today the public as well as the medical profession is being alerted and made to fear rheumatic fever. Through lectures and magazine articles parents are learning the dangers which may be associated with pains in the legs or murmurs in the heart. Anyone who has conducted a rheumatic

fever clinic is familiar with the experience of seeing a parent carry a healthy-looking child into the reception room, bringing with her a note from a school physician indicating that her child should be examined for suspected heart disease. Such a parent is already convinced that her child has heart disease. She takes a lot of talking to before she can be unconvinced and made to realize that her child has a normal heart; that the murmur means nothing and that the child may walk home, or run, if he will.

A physician assumes a grave responsibility if he tags a child with a diagnosis of rheumatic fever or rheumatic heart disease—a disease which carries serious implications for the child's future well being. At the same time, it is a decision which must be made without the help of a specific test. Modern medical science has developed so many diagnostic tests that a physician often feels at a loss when confronted with a situation in which specific laboratory confirmation is not possible. In any well equipped medical center there would be little chance of a diagnosis of syphilis without a positive serologic test, a diagnosis of diphtheria without finding a diphtheria bacillus or a diagnosis of active tuberculosis without finding a tubercle bacillus. We have, in fact, learned to lean so heavily on the laboratory, that the art and skill of "bedside" diagnosis has in many respects suffered the atrophy of disuse.

A diagnosis of rheumatic fever cannot be made by a laboratory technician. Its confirmation depends on the experience and acumen of the physician in differentiating the abnormal from the normal. It seems almost too obvious to mention that before abnormal signs can be properly evaluated, it is essential to have a thorough understanding of the normal. But it is a fact that an understanding of the normal has been grossly neglected in respect to at least two of the manifestations of rheumatic fever: aches and pains in the joints and cardiac murmurs.

Of the many manifestations of rheumatic fever, that pertaining to the joints may be discussed first since this is the symptom which has given the disease its name. In England the disease is still called acute rheumatism. This is an unfortunate choice of words for two reasons: first, although the disease has acute episodes, it is more chronic than acute; second, the term rheumatism is a vaguely used term often referring to the arthritedes of older patients. Arthralgia is a term frequently preferred in order to avoid confusion with rheumatoid arthritis. Characteristically several joints are involved. Usually the larger joints such as ankles, knees, hips, elbows and shoulders are affected, often in succession. Rheumatoid arthritis on the other hand is more apt to involve the small joints of the fingers and does not so often migrate from one joint to another. In typical rheumatic fever it is not unusual to see an ankle involved one day, followed by a wrist or elbow the next day. Hence the term migratory polyarthritis is frequently used. In a typical case the joint is swollen, hot and exquisitely tender. Active and passive motion are both painful. Other evidence of infection is usually present such as fever, leucocytosis and an increase in the erythrocyte sedimentation rate.

One of the characteristic features of rheumatic polyarthritis is its response to adequate doses of salicylates. This, as a matter of fact, is one of the dramatic therapeutic procedures which can be effected in the practice of pediatrics. A child who one day is suffering from extreme pain may after a matter of hours be made comfortable. It is important, however, to realize that the disease process itself is not affected thereby. This response to salicylate therapy is often very helpful in the differential diagnosis of rheumatic fever.

A typical case of rheumatic polyarthritis offers little difficulty in diagnosis but there are many borderline cases which may be confused with the so-called "growing pains" of childhood. There are those who maintain that all "growing pains" should be considered rheumatic manifestations. This, I believe, is unfortunate and may lead to unnecessary prolonged hospitalization of a child. One who sees a large number of healthy children in his practice is familiar with "growing pains" as a part of childhood which, although calling for investigation, may not be an abnormal finding.

In contrast to rheumatic polyarthritis which characteristically involves the joints themselves, "growing pains" are usually in the muscles of the legs—rarely in the arms. The pain of rheumatic polyarthritis is apt to be severe in the morning as well as throughout the rest of the day; "growing pains" occur at the end of the day, seldom in the morning.

Careful attention to the differential diagnosis of rheumatic polyarthritis and "growing pains" will, on the one hand, avoid over-diagnosis of minor symptoms in a normal child and, on the other hand, neglect of a serious situation.

Even more important is an accurate evaluation of cardiac murmurs. It is here that thorough knowledge of normal findings is of paramount importance. It is here that mistakes are so often made by

those familiar with the examination of an adult heart but not so familiar with the sounds of a child's heart.

In a child a murmur is more often than not a normal finding. Many studies have been done and reports presented of the per cent of apparently normal children found either by auscultation or phonocardiographic tracings or both to have functional systolic murmurs. One of the most recent of such studies is that of Epstein. This report is concerned with the cardiac findings in presumably normal infants and children who were under close medical supervision for an average of 5 to 14 years, many from birth. The study group consisted of 260 patients who were selected from a larger group of 416 patients. From the larger group all children were excluded who had any evidence of rheumatic infection, congenital cardiac anomalies, anemia, or cardiac enlargement. Of the children followed during the first 7 years of life, 52% presented precordial systolic murmurs during the period of observation. The majority of these children continued to show murmurs in subsequent years (up to the age of 14 years).

Another study on the occurrence of innocent adventitious cardiac sounds in childhood has recently been made by Friedman, Robie and Harris [unpublished data]. They subjected a group of 500 children between the ages of 2 and 12 years to special cardiac examination. Of these 500 children 234 (47%) were found to have functional cardiac murmurs.

If this high incidence of murmurs in the heart of normal children is kept in mind, serious mistakes in diagnosis will be made much less frequently. However, it must be admitted that a differential diagnosis between these functional murmurs and those of heart disease is often difficult. The functional murmurs are usually soft in quality and best heard at the base over the pulmonic area. They may be heard diffusely over the precordial area but are seldom transmitted to the back. The murmur of mitral regurgitation on the other hand is usually best heard at the apex, and, if well developed, may be transmitted not only over the precordial area but to the axilla and the back. If an apical systolic murmur is accompanied by an apical diastolic murmur, the diagnosis of rheumatic heart disease is confirmed.

The murmur of aortic regurgitation should present no difficulties if it is kept in mind. It is a high pitched, blowing murmur heard immediately following the 2nd sound and maximal at the left border of the sternum at the 3rd interspace. It should be listened for with a diaphragm type of stethoscope with the child upright and leaning slightly forward. Aortic regurgitation is usually associated with mitral regurgitation but occasionally may occur alone. When it does occur alone it can rather easily be confused with the murmur of a patent interventricular septum or a patent ductus arteriosus unless careful attention is given to timing the murmur. Both these murmurs are heard best along the left sternal border, but, whereas the murmur of aortic regurgitation occurs early in diastole, that of a patent interventricular septum is a harsh blowing murmur occurring during systole.

Any patient suspected of having rheumatic heart disease should have an electrocardiographic tracing but again it is important that too much weight should not be attached to slight deviations from the normal. The duration of the P-R interval has proven to be a useful guide; nevertheless, in recent years, we have learned that normal individuals not infrequently have a P-R interval longer than the usually accepted limit of normal. Furthermore it is important to bear in mind the fact that the P-R interval decreases with increasing pulse rate and with decreasing age of the patient. In the series of normal children in the report referred to above, the average P-R interval was 0.14 ± 0.02 sec. In the 1st year of life the value was 0.12 ± 0.20 sec. and 0.13 ± 0.20 sec. during the age span of 1 to 3 years. A useful although somewhat more elaborate table of normal P-R intervals which takes into account the two factors—age and pulse rate—is given in the textbook of Ashman and Hull.

Occasionally one encounters a patient with rather equivocal symptoms or signs of rheumatic fever in whom there is definite and persistent prolongation of the P-R interval. The question then arises as to whether or not we are dealing with delayed auriculo-ventricular conduction due to rheumatic heart disease or to a congenital cardiac defect. For such cases the response to a dose of atropine may be helpful in the differential diagnosis.

It has been shown that delayed A-V conduction of rheumatic heart disease can be decreased or abolished by the administration of atropine. This has been explained on the basis that the drug counteracts the effect of an increased vagotonia, and that the interference in conduction is therefore on a neurogenic basis rather than due to inflammatory changes in the system.

When confronted with a child in whom the diagnosis of rheumatic fever has been suggested,

where the history is equivocal, the findings of active infection absent or doubtful and the cardiac findings borderline, a prolonged P-R interval may add weight to a positive diagnosis. However, when the possibility of a congenital cardiac lesion is to be considered it is desirable to have further methods to differentiate a structural from a functional block. This should theoretically be feasible if the vagotonic impulses can be obviated. Under these circumstances in congenital heart block no appreciable change in conduction time should be noted, while in functional block the increased conduction time should be reduced to normal limits.

A series of unpublished observations were made several years ago at the Children's Hospital of Boston to demonstrate the usefulness of atropine as a differential diagnostic test. In a limited number of cases of well established rheumatic fever with P-R intervals varying from 0.04 sec. to 0.02 sec. above upper limits of normal, there was a decrease of 0.06 and 0.05 sec. to well within normal limits following the intravenous administration of atropine sulphate 1/120-1/75 grain. In other cases with congenital anomalies of the heart and prolongation of the P-R interval, there was no appreciable change in the P-R interval following atropine.

When rheumatic heart disease has reached the point of causing congestive failure there is usually no doubt about the diagnosis. Signs and symptoms at this stage of the disease are of significance from the point of view of following the course of the disease. One of the first and most easily detected signs of congestive failure in the child is the enlargement of the liver. Other signs of congestive failure occur in the child as they do in the adult: dependent edema, dyspnea, orthopnea, cyanosis, limitation of vital capacity, delayed circulation rate, increased venous pressure, decrease in urinary output and increase in weight.

A friction rub is, of course, diagnostic of pericarditis and usually offers no difficulty if one is on the alert for its occurrence. A pericardial friction rub or pericardial effusion are serious manifestations of the disease which indicate an unfavorable prognosis.

One manifestation of rheumatic fever which is often overlooked is abdominal pain. This is not infrequent and may occur before any other sign or symptom. It is frequently confused with acute appendicitis. Sometimes it may be impossible to make an accurate differential diagnosis particularly in the absence of other manifestations of rheumatic fever. In this connection the sedimentation rate may be helpful since it is not usually so elevated in acute appendicitis as in acute rheumatic fever. If abdominal pain is kept in mind as a possible early symptom of rheumatic fever unnecessary surgery may be avoided.

The subcutaneous nodules of rheumatic infection are pathognomonic with the exception that similar nodules may be found in rheumatoid arthritis. The nodules of these two diseases are distinguishable only by careful histologic examination and then only with difficulty. For the most part they occur in patients with severe rheumatic infection and extensive cardiac involvement, patients in whom the diagnosis is no longer in doubt. These nodules are not attached to the skin, but lie in the subcutaneous tissues so that the skin can be moved freely over them. They appear on the bony prominences of arms, legs, and shoulders. They may also occur on the extensor tendons of the hands, on the scalp, at the margin of the patella and over the spinous processes of the vertibrae. The frequency with which nodules are reported is closely related to the diligence with which they are sought, for they can be very easily overlooked.

Patients with nodules are apt to have from time to time erythema marginatum. Despite the fact that the rash of rheumatic fever is frequently loosely termed erythema multiforme it is in reality very distinctive and, like the typical nodules, seen only in rheumatic fever or rheumatoid arthritis. It is characterized by a narrow pink wavy line which tends to form a circular pattern. It may best be described as similar to the effect caused by marking the skin with a red crayon. Neither nodules nor rash cause the patient discomfort.

Chorea may or may not be associated with other evidence of rheumatic infection. This even more than other manifestations of rheumatic fever is a disease of childhood. It is seldom seen beyond the childhood years. Since it is usually so readily recognized it will not be discussed further at this time.

As stated at the outset, the laboratory is of very limited usefulness in the diagnosis of rheumatic fever. Determination of antistreptolysin titers may sometimes supply useful information in demonstrating that there has been a recent invasion of hemolytic streptococci, but this test can in no sense be considered specific for rheumatic fever. A more hopeful test is the antihyaluronidase test described

by Harris and his associates. It is too early to look upon this as a test which will solve our many diagnostic problems but the results to date look very encouraging.

The use of the sedimentation rate in following the course of a patient with rheumatic fever is so well known that it deserves little comment. It is, however, well to emphasize the fact that although nonspecific it is the most sensitive available index of continued infection. Any physician who is caring for a rheumatic patient should consider facilities for sedimentation rate a necessary part of his equipment. It matters little which method is used.

In summary it may be stated that in the absence of a specific laboratory or clinical test the diagnosis of rheumatic fever depends upon a thorough knowledge of the disease. Despite the vagaries of its many manifestations a reliable diagnosis can be made more often than not. And finally, perhaps the most important point of all, "growing pains" or functional cardiac murmurs must be recognized as normal findings in a growing child in order to avoid over-diagnosis and the unfortunate but not uncommon transformation of a normal child into a chronic invalid.

Treatment of Active Rheumatic Fever and Prevention of Recurrences

Dr. Jackson.—Considerable controversy exists regarding the treatment of active rheumatic fever and prevention of recurrences. Differences of opinion are to be expected until we have additional knowledge to explain the protean manifestations of the disease. We have to admit that no specific treatment is known. The object of this presentation is to focus attention on the child with rheumatic fever and his family, and to discuss current methods of therapy.

Many types and various phases of the disease have been described. The chief manifestation of rheumatic fever in children regardless of clinical type is carditis. As is well known an outstanding characteristic is its tendency to recur. For purposes of discussion the disease can be divided into 5 phases: (1) the phase of invasion of the inciting agent, (2) the phase of latency between invasion and the development of symptoms and signs, (3) the phase of rheumatic activity, (4) the prolonged phase of quiescent activity and (5) the phase of rheumatic inactivity.

A child with rheumatic fever may come under observation in any phase of the disease. A detailed medical and social history and complete examination are essential in order to evaluate the patient as well as the disease. When adequate facilities are available, with few exceptions, hospital care is indicated to evaluate properly the patient and his family and to help them adjust to the situation and to plan for the future care of the child. Although the child may be in need of hospital facilities he is in need also of emotional security and great care must be taken not to separate him precipitously from his family.

Treatment should be prompt and intensive in the hope of preventing disabling heart disease and cardiac decompensation and of modifying the duration of the attack. Too frequently adequate care is obtained only after the patient's condition has become critical because of progressive cardiac involvement. Early treatment and a long range plan of care have proved to be not only the best safeguards for lowering morbidity and mortality rates but also provide an opportunity for the child and his family to obtain professional guidance.

Emotional Care

The detrimental effects of severe anxiety on the various physiologic functions of the child are well known. His body musculature may be under tension leading to unnecessary energy expenditure and fatigue; depression in mood may result in poor appetite; unresolved anxiety may lead to terror dreams and restless sleep. Attention must be paid to the basic sources of anxiety. The child fears, above all else, separation or emotional estrangement from his parents. There is always the possibility that the child will interpret his illness as punishment for real or imagined misconduct and if, at the time of hospitalization, he is abruptly separated physically from the parents, the most effective source of reassurance has been removed. Many of the children are emotionally estranged from their parents, and good therapy must include the provision of adequate parent substitutes who can help the child feel accepted and loved. All children fear mutilation to some degree, and harbor many fantastic concepts of what may happen to them in a strange situation. The doctor must realize that such fears may exist, and carefully guard against discussion of heart disease and operations or other dangerous sounding procedures (often couched in ambiguous technical terms which arouse anxiety) in the patient's presence. Each procedure which is done should be fully explained and the

child given a reasonable opportunity to ask questions. After a painful procedure, he should be given an opportunity to express his resentment verbally or through play with the approval of the doctor. Variation in emotional care of patients is one of the major uncontrolled factors not taken into consideration when evaluating the results of therapy.

Rest

It is universally conceded that during the active stage of the disease the child's most urgent need is bed rest. Complete bed rest, although routinely requested by the physician, is approached in varying degrees with each patient. To attain such degrees of rest much more is required of a hospital than a clean bed, quiet sunny surroundings, a daily bath with tepid water and controlled temperature and humidity. While these are all very important the child also needs to realize that he is in a good place where everyone in attendance is interested in him and that his family wants him to be in the hospital. A type of highly individualized care is required which necessitates a well-trained hospital staff that has the patient's interest at heart and is willing to give of itself for the welfare of the child.

Sedatives frequently are useful in providing physical rest for the child. If adequate physical and emotional care is provided, sedatives should not be required for any extensive period of time. Because bed rest is difficult or impossible to provide in the homes of many patients with rheumatic fever and in too many hospitals, it is not surprising how frequently it is carried out half-heartedly or not at all. Variation in the amount of rest is a major uncontrolled factor not taken into consideration when evaluating the results of therapy.

Nutrition

The nutritional care of the child with rheumatic fever is extremely important. To a great extent the same situation exists regarding diet as with bed rest in that the nutritional requirements are approached in varying degrees with each patient. In working out a diet for the child with rheumatic fever we must keep in mind not only the child's nutritional needs but also his physical condition and his food likes and dislikes. The food should be prepared and offered in such a way that mealtimes are pleasant and that his participation in selecting the foods is educational. Mealtimes under such a regimen can become an interesting learning project rather than a tiresome routine which may result in serious feeding problems. The physician too frequently simply advises the mother to give the child nutritious foods, or, in the hospital, writes routine diet orders. The family background and the child's eating habits are often completely ignored. Routine trays providing protective and even fortified foods are of little avail if the child is unable or refuses to eat the food. Forcing of the food by the nutritional or nursing staff only complicates the situation. The importance of understanding personnel again becomes obvious.

The child with active rheumatic fever invariably is in a poor nutritional state and has anorexia. Small frequent feedings are preferred to routine meals. The diet should be low in fat because of the anorexic effect of fat and the inability of sick or malnourished children to absorb fat well. The diet should be high in protein content because the patient is to a greater or less extent in a state of protein depletion and the sick or malnourished child's ability to absorb and utilize protein is good. Carbohydrate foods are well utilized and afford the easiest means of maintaining an adequate caloric intake.

The mineral requirements are best met by including one quart of skimmed milk in the diet and providing 10 to 15 mg./day of iron either in the foods or as inorganic salts.

The intake should include at least vitamin A 5,000 u. and vitamin D 400 u./day. The water miscible forms of these fat soluble vitamins are known to be absorbed more readily than oily preparations. It has been found that children with active rheumatic fever have a low blood vitamin A level. At present we are attempting to determine the vitamin A requirements of such children. The vitamin D requirement is stated to be increased in children under nutritional stress; however, studies in our laboratory tend to show that such children recover nutritional efficiency slowly, and that recovery is as prompt with lower levels of vitamin D and a fully adequate diet, as when high levels of vitamin D are included.

It may be that the vitamin A and D requirement of these children is well above that of the normal child. Very large dosages of vitamin A or D are not yet warranted and, with our present

limited knowledge, should be avoided, because fat-soluble vitamins are stored in the body and excessive intakes give rise to later manifestations of toxicity. Many studies have been done to determine the vitamin C requirements of the child with active rheumatic fever. The child should receive daily at least 100 mg. of ascorbic acid per day, preferably in foods. If the child's intake of protective foods is ample he will receive a sufficient intake of the water soluble vitamins. However, when the food intake is limited in the more active phase of the disease, vitamin B preparations are indicated and should be given to about double the allowance recommended by the Food and Nutrition Board of the National Research Council for normal persons.

The food intake should be evaluated daily and every effort should be made to meet the nutritional needs of the child.

If the child has signs of cardiac decompensation, sodium restriction is indicated (1 to 3 gm. daily). The only sodium permitted is that contained in the protein foods. The water intake is not restricted.

The value of blood transfusions for the child with active rheumatic fever and hypochromic anemia has not been sufficiently studied. Small repeated transfusions given slowly have been routinely used in our hospital without apparent harm and often with dramatic results. Even signs of decompensation have not been considered as contraindication for transfusions if the hemoglobin value is less than 9 gm./100 cc. Washed blood cells might be preferable but the value of the plasma for nutrition must be considered. Further research in this area is indicated. We have not used concentrated glucose, although this type of therapy has been recommended in conjunction with insulin. There is no evidence to support the use of insulin in conjunction with parenteral administration of glucose for children with rheumatic fever. The fluid requirements of the child must be met. An isotonic solution of glucose may be administered slowly for this purpose. Adequate fluid intake is extremely important in avoiding toxic effects from salicylates and digitalis.

The Salicylates

Only the salicylates have survived the test of time in the treatment of rheumatic fever. Salicylate therapy has been in use for over a half a century and opinions have varied among clinicians as to the mode of action and the value of salicyl compounds. Most authorities agree that the salicylates have analgesic and antipyretic action. Few, however, have felt that salicylates modify the progress of the disease. Tremendous interest has been aroused, therefore, by Coburn's recent report that by means of massive doses of salicylates cardiac sequelae could be modified, if a level of blood salicyl (measured as salicylic acid) above 350 μgm./cc. is maintained. According to this author, the failure of salicylate therapy in the past may have been due to inadequate dosage.

Numerous reports of salicylate poisoning in children with rheumatic fever have appeared in the literature since higher dosages have been employed as advocated by Coburn. Hyperpnea, anorexia, apathy and lassitude are the important early signs of salicylate intoxication in children. Hyperventilation is believed to result from a disturbance of the respiratory center and causes respiratory alkalosis. The diagnosis of respiratory alkalosis as of respiratory acidosis is dependent on the estimation of both the total plasma CO_2 content, plasma Cl, and plasma or urine pH.

Dubow and Solomon have recently studied salicylate tolerance and toxicity in children and find that sodium salicylate given in divided doses over a 24 hour period (.85 grain per pound of body weight) resulted in therapeutic blood levels without toxic symptoms and with normal serum CO_2 content and pH values. Acetylsalicylic acid gave slightly higher blood levels than the sodium salt. Salicylates were found to be tolerated less well by acutely ill than mildly ill or convalescent children. When physiologic function was deranged, even small doses resulted in very high blood levels. Adequate fluid intake and renal function were major factors in preventing retention of the drug.

The simultaneous administration of sodium bicarbonate with salicylates results in a lower serum salicylate level. A recent study by Hoffman and Nobe showed that the excretion of salicylate in the urine is proportional to the pH of the urine and that the excretion of salicylate is dependent upon the amount of fixed base available for the excretion.

Hypoprothrombinemia induced by salicylate was first demonstrated by Link, Overman, Sullivan, Huebner and Scheel. These authors fed salicylate to rats deficient in vitamin K and many of the animals so treated died with hemorrhagic manifestations. Recent studies have shown that similar effects have occurred in humans even though they have shown no previous vitamin K deficiency. Meyer and Howard have reported that vitamin K will protect completely against the reduction in

prothrombin if it is given in conjunction with salicylate. Shapiro estimated that approximately 1 mg. of synthetic vitamin K will counteract the prothrombin reducing action of 1 gm. of acetylsalicylic acid.

Taran and Jacobs have shown that the oral route of administration of salicylate is as effective as the intravenous route and that the intravenous route is hazardous. They found large doses of salicylates to be very effective in controlling the exudative manifestation of the disease.

In our experience children have tolerated acetylsalicylic acid well. It has not been necessary to use sodium bicarbonate to prevent gastric irritation. Our present policy is to use acetylsalicylic acid .8 grains/kg. body weight/24 hours divided into 6 doses and to carry out blood levels studies if any suggestive symptoms or signs of intoxication are noted.

There can be little doubt that most children with active rheumatic fever are benefited by the administration of salicylate in doses sufficiently large to lower the temperature and alleviate discomfort. When his sense of well being improves he is more comfortable, becomes more hopeful and more co-operative, his appetite improves and he can rest better. Whether the salicylates per se or their secondary effects modify the course of the disease is of academic interest. It must be remembered, however, that the drugs must be administered cautiously, calculating the dosage on the basis of body weight and clinical status of the child and with due regard for the acid-base changes and hypoprothrombinemia which they may produce. It would seem wise to avoid massive doses of salicylates if the child must be treated where laboratory facilities are limited.

Digitalis

Controversy continues as to whether digitalis produces more toxic than therapeutic effects for the failing heart of the child with active rheumatic carditis. In my opinion and experience there is more evidence to support than to condemn the use of digitalis during impending or definite cardiac failure. We must remember that digitalis is not an anti-rheumatic drug, and that the child may become worse with cardiac failure increasing even when full therapeutic doses of the drug are given. The dosage must be calculated accurately on the basis of corrected body weight and the fluid exchange of the body must be kept in mind. The most frequent error lies in increasing the dose until toxic symptoms and signs appear. Best results are obtained when small frequent doses are given and a plan is followed which does not vary significantly from patient to patient. Although serial electrocardiographic tracings are helpful in detecting early signs of toxicity (especially toxic rhythms), their utility is limited. In the majority of cases it is safe to assume that the child has had enough digitalis if there are fairly marked depressions of the R-T segments with deep inversion of the T-wave.

Since many glucosides are becoming available for clinical use the problem becomes more complicated as to the selection of a particular glucoside as the one of choice. Obviously children with active rheumatic carditis and congestive cardiac failure are not desirable subjects for preliminary studies. A standard preparation of digitalis (0.1 gm. = 1 cat unit) in the dosage of 0.02 gm./kg. of body weight for a full digitalizing dose is to be recommended. Half of the calculated amount is given for the first dose and the remaining half is given in 4 doses over the remainder of the 24 hour period. A maintenance dosage of approximately 0.05 gm./day is administered in 4 doses and the dosage adjusted according to the response of the child and the findings of repeated electrocardiographic tracings.

Oxygen Therapy

Oxygen is of definite benefit to the child with rheumatic pneumonitis or congestive cardiac failure. Oxygen should be given early and as long as the patient's respirations are labored. The method of administration will to a great extent depend on facilities at hand. Few hospitals have facilities comparable to those described by Taran. This author's recent studies show that established cardiac damage cannot be reversed by oxygen therapy and that the direction of the rheumatic activity is not measurably altered, but that oxygen therapy is an important form of treatment in active rheumatic carditis of the exudative type with minimal mechanical cardiac disabilities. In our experience the oxygen box or tent with transparent sides is better tolerated by the child than the nasal tube. The child should be psychologically prepared by the physician before oxygen administration is undertaken and the nurse should be in constant attendance until all fear of the apparatus is dispelled.

Diuretics

Diuretics are indicated when there are signs of cardiac failure. The mercurial diuretics (mercupurin or mercuhydrin) have been most effective in our experience. Mercupurin or mercuhydrin is administered in frequent small doses intramuscularly until evidence of congestive failure and active carditis has subsided.

Other Drugs

Chemotherapeutic or antibiotic drugs such as sulfadiazine or penicillin are ineffective during the active phase of the disease. There is evidence that sulfonamides administered during the active phase may cause exacerbation of signs and symptoms. Penicillin apparently has no effect on the course of the disease and would therefore be preferable to sulfonamides in treating a superimposed bacterial infection which would respond to either drug.

We have had no experience with other drugs, such as succinic acid, benzyl ester, para-aminobenzoic acid and gentisic acid which are being studied as possible substitutes for salicylates. It is hoped that research in this area will clarify the action of these drugs and advance our knowledge of the pathologic physiology of rheumatic fever.

The child with chorea presents a special problem from the therapeutic standpoint. Often carditis and other signs of rheumatic fever are absent. In fact, there is still reason to doubt if chorea is a manifestation of rheumatic fever or whether it may be a separate entity which breeds under common environmental conditions. The importance of a complete social history and psychologic evaluation of the child cannot be over-stressed in the management of Sydenham's chorea. In our experience serious social problems almost invariably are found in this group of patients. Treatment consists of the use of sedatives but as previously stated the sedatives should not be required for any extensive period of time if adequate emotional and physical care are provided. Adequate emotional care frequently requires psychiatric consultation.

We have been discussing the treatment of the rheumatic child during the active phase of his disease. When the disease becomes quiescent, or is in the 4th phase, he will require weeks or months of convalescent care before he can be allowed to resume physical activity. Convalescent care is best given in a sanatorium where there are adequate facilities to meet the physical, emotional, intellectual and spiritual needs of the child. The child should remain under the regimen of convalescent care until his disease is definitely arrested and then activity should be resumed gradually. The child who has spent his quiescent phase in a convalescent home or ward after he has proved that he can endure limited physical activity without any signs or symptoms of cardiac embarrassment is ready to be discharged to his own home. Concurrent with the care of the child is the education of the community to help the parents establish a wholesome environment for the patient and other members of the family.

As I stated in the beginning, when the rheumatic child comes under medical care the home environment of the child should be evaluated by an experienced and understanding medical social worker. When it is found inadequate, as it most frequently is, work on raising the level of the environment should be started immediately. In our clinic special emphasis is placed on insuring a good dietary for the child and for his family. This, however, is not the only phase of family rehabilitation that is undertaken. When the family social situation is poor, great effort is made to improve it too. In short we try to insure a good environment for the rheumatic child to live in. It is our feeling that this is the important protective factor against recurrence of the disease and in many instances it is the only one the rheumatic susceptible child will need.

The family of each child is instructed by the doctor and nurse and often by a dietitian regarding the importance of an adequate diet which should include the daily consumption of: one quart of milk; one or two eggs; one serving of meat, fish, fowl, or liver; two vegetables ($\frac{1}{2}$ cup is considered a medium serving); one orange, apple or tomato; one other fruit in addition; one teaspoonful or equivalent of cod liver oil; six teaspoonfuls of butter or margarine. They are also told that other foods such as bread, cereal, and potatoes can be added to satisfy the appetite and maintain correct weight, but in no circumstances are they to replace any of the above; cereal is not to be served more than once daily. Rather, the child is to be encouraged to eat larger quantities of fruits and vegetables; varieties of these are to be used, so the child will not form likes and dislikes.

Each family is advised to have the child sleep in a room of his own whenever possible or at least to sleep alone, and to have about 10 hours of rest each night. The importance of proper

clothing is stressed, as well as control of temperature and humidity of the home. With regard to the care of intercurrent infection, the family is advised to have the child go to bed if there is any sign of infection, and to consult the family physician as early as possible. If another member of the family has a cold, sore throat or any other infectious disease, the child is to be kept away from that person and the family physician notified. The family is told to have the child play with other children in the normal way, but to plan his activities to avoid fatigue. In addition, psychologic advice is given to prevent over-protection. The importance of persevering with a high level of care day after day and year after year is emphasized and re-emphasized at each clinic visit in his medical follow-up care.

Many of the children with rheumatic fever living in Iowa come under the care and supervision of the University Hospital and the clinics of State Services for Crippled Children held throughout the state. The recrudescence of rheumatic fever among 266 of these children has been studied recently by us. This study was undertaken to determine the recurrence rate of a group of rheumatic subjects who have received special attention to improve their diets and level of environmental care. Many of the observations of the study (onset of the disease 1930-1946) were made prior to the use of sulfonamide prophylaxis by anyone and we had not used sulfonamide drugs although many clinics have used them the last few years.

The 266 patients of the Iowa study group were under observation a total of 893.5 person-years from 4 to 21 years of age. The age specific recurrence rate* was obtained. For the age period 4 to 13 years there were 37 recurrences and 3 deaths for 504.5 person-years of observation or a rate of 7.9% for the age period 14 to 16 years, there were 24 recurrences for 233.5 person-years of observation, or a rate of 10.3%; for the age period 17 to 21 years, there were 7 recurrences for 155.5 person-years, or a rate of 4.5%. For the total group, 71 major and minor recurrences were experienced by 51 children.

The recurrence rate of rheumatic fever in this study group of rheumatic subjects who received special attention to improve their diets and level of environmental care is significantly different from that reported by Wilson for a random sample. The recurrence rate for the study group is lower for the age group 4 to 13 years and slightly higher or the same for the older age groups. It is noteworthy that the age 4 to 13 years is a period in which the nutritional requirements of the child are high and a time in the child's life when his habits of living can be controlled with less difficulty than from approximately 14 years and older.

In a study of the rate of recurrence of rheumatic fever within one year of the previous attack for children 4 to 16 years of age the rate of an Iowa control group and Iowa treated group was compared. The rate for the control group was significantly higher than the rate for the treated group and did not differ significantly from the rate reported by Wilson for recurrences within one year of previous attacks.

Of the 51 children who had recurrences 13 children who had recurrences with carditis comprise a group that suffered the serious effects of the disease. An analysis of their histories and environmental care shows that 3 of these children died within 2 months of their discharge from the sanatorium, and, in retrospect, there is doubt as to whether their disease was inactive. Their environmental care was fair or better, except for one boy who lived in a poor social situation. The 10 children who survived with carditis, on the whole, lived in a poor home environment; all lived in poor social situations, 7 in very limited economic circumstances, 7 on a poor and 3 on a fair dietary regimen.

In recent years a number of clinics have used sulfonamide prophylaxis and have reported successful results in the prevention of recurrences. The recurrence rate for major episodes for the accumulated reported groups of rheumatic patients who have received sulfonamide prophylaxis is 1.5%. These reports show that the drugs do have prophylactic value. The reported number of toxic reactions show the sulfonamide drugs to be by no means harmless. In addition to the toxic reactions from chemotherapeutic or antibiotic agents, there is also the danger that the host may lose his ability to resist the organism and also the bacteria may become resistant to the drugs. Quinn reporting recently an epidemiologic study of rheumatic fever in Navy training centers states that "At one

* The recurrence rate for a specified age period is the number of recurrences during the specified period divided by the number of person-years observed during the specified period. The quotient is multiplied by 100 to express in terms of per cent.

time the Navy was faced with a desperate situation wherein epidemics of hemolytic streptococcal infections were a grave menace to the training program. Because of the seriousness of the problem prophylaxis with sulfonamide compounds was instituted. The incidence of streptococcal infection was reduced dramatically and at the same time the rate of rheumatic fever fell; these reductions, however, were only temporary. Later, certain strains of Str. hemolyticus acquired resistance to the sulfonamide compounds and the incidence of infection by these organisms returned to epidemic proportions. Similar experiences were observed in the other Navy and Army establishments." Baldwin reported that her observations on rheumatic children receiving sulfonamide prophylaxis while at home showed no appearances of any sulfonamide resistant strains of streptococci.

A review of the histories of the 266 Iowa rheumatic children showed that if the disease is definitely inactive, an excellent diet and wholesome living conditions will practically eliminate the chances of a recurrence with carditis. It is my opinion that sulfonamide prophylaxis is indicated for only those children recovered from rheumatic fever who have definite rheumatic heart disease and are forced to live in an environment which does not provide a good diet and at least a fair level of general care. It is possible that oral penicillin may prove to be safer and as effective as sulfonamide prophylaxis.

Special mention of our experience with chorea might be made here. Chorea is a type of manifestation we found most difficult to prevent, and it accounted for approximately 1/6 of the recurrences. Of the 12 children with recurrences of chorea the social evaluation of the home situation was available on 10. Of these, 4 were poor or poor to fair, 5 were fair, and 1 was good. That is, for only one child with a recurrence of chorea was the home situation considered good, and the remaining 9 were marginal or worse. An attack of chorea may be precipitated by emotional strain or psychological trauma experienced by the child in his home and sometimes in his school environment. In view of this impression I advise an investigation of the home social situation and rehabilitation, and an investigation into any school problems with interviews with his teachers before he returns to his home and school environment.

For the child in whom rheumatic fever has been inactivated, and for any child, the treatment of infections is most important. It is during this phase of the invasion of the beta Str. hemolyticus. that we must watch and give adequate medical care to make certain, if possible, that the child has completely recovered from the infection. With an invasion of beta Str. hemolyticus the rheumatic susceptible child is in grave danger of another cycle of rheumatic fever being initiated. Many attacks of rheumatic fever including first attacks might have been avoided if the child, when he first became a victim of an acute infection had been put to bed, given good medical and nursing care and kept in bed until all signs and symptoms of active infection had disappeared. While I have not endorsed giving sulfonamide prophylaxis routinely, when there is an epidemic of beta Str. hemolyticus, the rheumatic susceptible child should be given sulfonamide prophylaxis under the supervision of a physician. What I would avoid is giving sulfonamides routinely and continuously and by this dangerously simple device thereby neglecting the possibilities and benefits derived from improvement of the child's health by adequate dietary and better living conditions.

Children with rheumatic fever most frequently come from impoverished and disrupted homes. The disease tends to breed in families where serious longstanding social problems exist. The economic factors are secondary in importance to the sociologic factors, because our society has ways and means of helping the needy. Students of rheumatic fever cannot fail to learn how important wholesome family life is to the welfare of children and how devastating immoral practices such as selfishness, greed, alcoholism, promiscuity and divorce are to wholesome family life. Only when an attack on these very complicated detrimental forces is made, utilizing supernatural and natural resources, can we hope for the eradication of this scourge of childhood.

Chairman Hill: We have a large number of questions to answer, and many of them, of course, involve discussion of the same factors. One of the most common questions that has come up has been a discussion of the electrocardiographic changes reported by Dr. Parr in a recent publication. I think I will ask Dr. Hubbard, Dr. Jackson and Dr. Harris, all three, to comment on that. Do you want to start in, Dr. Hubbard?

Dr. Hubbard: We have a number of questions about the value of the Q-T interval.

Some years ago I followed a number of electrocardiographic tracings.

In my experience the prolongation of the Q-T interval was not a very significant finding, and we did not find it of much value in the diagnosis of the disease or following the course of it.

Chairman Hill: Dr. Harris, would you comment on that?

Dr. Harris: I agree entirely with Dr. Hubbard on that.

The electrocardiograph is not nearly so useful to us as to people who see cardiac disease in adults. The occasional case which Dr. Hubbard mentioned before is about the only electrocardiographic sign of acute rheumatic carditis worth bearing in mind.

Dr. Jackson: Prolongation of the Q-T interval theoretically should be a reliable index of active myocarditis. At the present time we do not have sufficient data to evaluate this sign in our patients.

Chairman Hill: Dr. Wheatley, do you have a question?

Dr. Wheatley: There is a question here, "Is there any evidence that the incidence of rheumatic fever is diminishing since the advent of chemotherapy?"

It is difficult to answer this question because I know of no study of this precise question. We have some indirect evidence that the severity of the disease, if not the disease itself, may be decreasing. If you will accept mortality as a measure of severity, we know that the trend in mortality from rheumatic fever and rheumatic heart disease in the general population in children has been going down for as far back as 1910.

On the point of whether or not chemotherapy and antibiotics have had any possible influence on the mortality from rheumatic fever and rheumatic heart disease, we studied our industrial policyholder mortality. The number of insured in the ages 5-14 have been of the order of millions and not thousands so that the numbers are large enough to be significant and representative of the child population in cities.

The mortality in the seven years prior to 1940 was compared with the mortality for the seven years since 1940. The year 1940 was considered the year when sulfa treatment of streptococcus infections and other acute illnesses amenable to sulfa therapy might have been in general use among the medical profession. Prior to 1940, the percentage reduction in mortality from rheumatic fever and heart disease was of the order of 22% in children from 5 to 14.

In the seven years since 1940 the rate has been three times faster. It is about on the order of 65 to 66%.

This significant improvement may be due, in part at least, to the radical improvement in the treatment of streptococcal infections which has occurred with the use of the sulfa drugs and more recently penicillin. The precise way that this reduction in the duration and severity of streptococcal disease may have reduced the severity and possibly the incidence of rheumatic fever cannot be explained until we clearly understand the chain of biological events which produce an attack of rheumatic fever.

Chairman Hill: This morning, when we were getting together to discuss the panel, we spent considerable time talking about the subject of growing pains, and I am sure we were not the only ones interested in the subject of growing pains by the number of questions that have come up. Here is a typical one:

"Is there actually an entity such as growing pains, and, if so, what is the etiology?"

"Etiology of growing pains; treatment and prophylaxis of growing pains."

I think there are some 15 or 20 others.

We will lump them together and perhaps ask various members of the panel to talk about what we mean by growing pains.

Dr. Hubbard: This question is: "Does it hurt to grow? If not, why speak of growing pains?"

I can give no positive etiology of growing pains. I think we are aware of the fact that they do occur mostly in the legs of children and perhaps are related to the stretching of the muscles and bones, but that is purely theoretical. Poorly fitted shoes should be considered.

Chairman Hill: Dr. Harris, can you enlighten us about the etiology of growing pains?

Dr. Harris: No, but it is a very annoying problem in any diagnostic clinic, such as the one we have at Philadelphia General Hospital. The only thing I can say is that unless such pains are a part of a definite infectious episode involving the body as a whole in an ill child, such as a child with a fever of 102° or so, it probably means nothing.

When a mother tells me her child has occasional episodes of that sort, I make sure the child comes in sometime within a week or so following such exacerbation of growing pains, and gets

erythrocyte sedimentation rate at that time. If that is normal, it is extremely doubtful to me that within a week previously there might have been an exacerbation of rheumatic fever.

Dr. Jackson: Growing pains commonly occur in young children (3 to 5 years) when muscular growth is rapid and in older children during their prepubescent growth spurt. The cause of these pains, as far as I know, is not understood.

Dr. Harris: Here are a few questions on the nature of "How complicated is the anti-hyaluronidase test?" and so forth.

Obviously, this is no point to go into the mechanism of a serologic test. Actually, it is perhaps a bit more complicated in the matter of reagents than other serum neutralization tests done in the laboratory.

We try to simplify our technics so as to make this test comparable to others, such as the anti-streptolysin tests. Our own reports are published in the American Journal of the Medical Sciences (February 1949) and PEDIATRICS (April 1949)—two papers, one on the basis of the test and one on the application. Some of the charts shown were from those papers.

It is essentially a question of preparing a hyaluronic acid from umbilical cords and preparing hyaluronidase from streptococcal cultures. Any laboratory in which there is enough interest can develop these technics, as it would for any serologic test.

Chairman Hill: We will switch to Dr. Jackson and ask him to report on some of his questions.

Dr. Jackson: The first question I have is: "Does salicylate cause acidosis or alkalosis?"

There have been a number of recent studies to show that accumulation of salicylates in the blood causes respiratory alkalosis or acidosis. The alkalosis usually is first and transitory. The diagnosis of respiratory alkalosis or acidosis is dependent on the estimation of both the total plasma CO_2 content, plasma Cl and plasma or urine pH. It would, therefore, seem wise to avoid massive doses of salicylates unless the child is treated where laboratory facilities are readily available.

Chairman Hill: Dr. Hubbard.

Dr. Hubbard: I have several questions relating to the use of atropine as a differential diagnostic test between prolongation of P-R interval due to rheumatic fever or to congenital heart disease.

The first question was asked as to the dose. We have used 1/75 to 1/120 grain and then taken electrocardiograms at frequent intervals.

I do not present this as anything more than a test which may sometimes be helpful. Too much reliance should not be placed upon it, but it may be useful in a case where other signs are equivocal and there is doubt as to whether a prolonged P-R interval may be evidence of a congenital or acquired lesion.

Chairman Hill: Dr. Harris.

Dr. Harris: There are two here that I might lump together. Both have some immunologic aspects.

One is: "If hyaluronidase is used in administering clyses, would this substance cause antibody response which would confuse the interpretation of antihyaluronidase study later, and could it cause undesirable effects because of the possible relationship to rheumatic fever?"

The amount necessary for increasing absorption in hypodermoclysis is minute, and I am quite sure that it would not excite any antibody response at all.

The other question is this: "In a yet unpublished work Cavelti has demonstrated precipitins in the blood of acute rheumatic patients by the collodion particle technic with fresh human heart as the antigen. Would you consider this as supporting evidence of the value of the collodion particle technic?"

The only thing I can say there is that the precipitin method does not measure the concentration of antibodies to a soluble antigen. In fact, the rationale for the beginning of the original work on collodion particle technic by Cannon and Marshall was the need for a method in which the serum is diluted, so that serum antibodies to a soluble antigen can be measured reliably. It is therefore impossible to assess the quantitative significance of antibody measurement by precipitin technic.

Chairman Hill: Dr. Jackson, you have several.

Dr. Jackson: The relationship to therapy in the acute phase first.

"Comparison of sodium retention (reduced urine sodium output) and diminution in vital capacity as indications of incipient cardiac decompensation in rheumatism."

Sodium retention and diminution of vital capacity are definite signs of cardiac decompensation. The determination of sodium retention by reduced excretion of Na in the urine, although theoretically

sound, would be impractical for ordinary clinical purposes. The patient's sodium and potassium intake would have to be known as well as the amount of fluids lost by sweating in order to interpret the values obtained by analyzing the urinary output. Vital capacity readings are very useful in older patients. The other clinical signs mentioned by Dr. Hubbard such as shortness of breath, liver tenderness, nausea and vomiting are invariably present. If decompensation is suspected, we usually give oxygen and diuretics and digitalis is administered as soon as the diagnosis is certain.

Chairman Hill: Dr. Hubbard, will you carry on?

Dr. Hubbard: I have several questions here related to the sedimentation rate.

One question is in regard to comparative methods—whether the Westergren test is preferable to one of the micro tests.

I think the important thing is not that one test is perhaps a little better than another, but that you should be familiar with some test in your own practice and know the normal for that particular method.

For example, in the Westergren technic, it makes a good deal of difference what anticoagulant may be used. It is obviously important, therefore, to know the normal for the test that you are using, with the various factors involved.

I think it has been pretty well demonstrated that for investigative work, a method which takes into consideration a correction for packed red cells is more accurate, but here again certain variables must be considered, such as the speed with which the centrifuge is running.

There is a question on the "Use of white blood cell count in following the course of the disease."

The white cell count is, of course, of value but of less value than the sedimentation rate.

Chairman Hill: Dr. Harris, do you want to answer that question in front of you, about the sedimentation rate?

Dr. Harris: This won't take long. It says: "How do you explain the normal sedimentation rate seen in acute cardiac failure when previous to decompensation the sedimentation rate has been elevated?"

The answer is: I haven't the faintest notion.

I do know that, according to Dr. Jones' estimates, in about half the cases where the sedimentation rate was very high, after decompensation the sedimentation rate paradoxically returned to normal, and there is no better evidence in the world of the aggravation of rheumatic carditis than cardiac decompensation. Since we don't know the mechanism for the increased rouleaux-formation that causes an increased sedimentation rate, and since we don't know the mechanism of the pathologic changes in rheumatic fever, I suppose we may be forgiven for not understanding this paradoxic relationship.

Chairman Hill: Dr. Hubbard, will you comment on that question?

Dr. Hubbard: This is an interesting question and points out this fact that in congestive failure the sedimentation rate may be normal or even considerably less than normal. A decrease in a previously elevated sedimentation rate may be a helpful sign of the development of congestion failure.

There is one more question, while we are talking about sedimentation rates: "Is an elevated sedimentation rate and pulse between 90 and 100 in a 5 year old child, with no anemia and no other symptoms, sufficient for a diagnosis of rheumatic fever?"

I would say very definitely that if all we have is some elevation of the sedimentation rate and a pulse rate between 90 and 100 in a 5 year old child, I certainly would be very reluctant to accept the diagnosis of rheumatic fever. One would want to look for other causes of the elevated sedimentation rate.

In regard to the pulse rate, we have found it very useful to take the sleeping pulse of the child in the evening and find it a much more reliable test than taking the pulse during the day when the child may be excited. The sleeping pulse rate of over 80 in a child is apt to be significant.

There is another question here in regard to the elevation of temperature: "Is there any proof that it is harmful for a child with a temperature of 99.2° to be out of bed or attend school?"

I would like to urge against overemphasis upon the slight variations from normal. Sometimes I think the best thing you can do for a parent who is wondering and worrying about a temperature of 99.2 is to tell her to throw away the thermometer.

Dr. Jackson: I would be glad to comment further in regard to this. We made a study a number of years ago to determine the variation between oral and rectal temperature readings. Although the rectal temperature reading was greater than the oral reading by an average difference of one

degree it was observed that the differences between the rectal and oral temperatures were not constant. Brennemann has reported definite elevation of rectal temperature following physical activity.

I heartily agree with Doctor Hubbard's comments. We must know where the temperature was taken and under what circumstances as well as the exact reading in order to make a correct interpretation.

I also have a question here on the sedimentation rate. It is the old proverbial question that invariably is asked, "Do you insist upon a normal sedimentation rate as a criterion of inactivity?"

If a child is convalescing from an attack of rheumatic fever and meets all the usual criteria of inactivity except a high normal or slightly elevated sedimentation rate, I would advise a careful investigation to determine if the child has a focus of infection. If no focus of infection is found I would gradually increase the child's activity under close observation.

Chairman Hill: Here is a question which sums up the group of questions concerning the child with low-grade fever. This is a problem familiar to all of us engaged in pediatric practice.

"A common problem met in practice in our community is that of the child over 6 or 7 years with a fever of 100° F. orally (with corresponding elevated rectal temperature) of 4 weeks' duration, complaints of anorexia, pallor, fatigue and perhaps occasional nosebleed, also moderately elevated sedimentation rate, essentially normal hemogram, and normal EKG. How would one rule in or rule out rheumatic fever?"

That, of course, is the problem of etiology of low-grade fever. We must consider that there are many possible causes of low-grade fever aside from rheumatic fever. Most of us have a routine which we put these patients through, such as blood count, sedimentation rate, urinalysis, tuberculin test and x-rays of the sinuses and nose and throat in addition to the history and physical examination.

In our experience we have more often found the cause of low-grade fever such as this to be somewhere in the respiratory tract, sinuses, tonsils and adenoids, or cervical glands. Rheumatic fever has been a rather uncommon finding in our experience in children of this type.

I would like to ask Dr. Jackson to comment on this particular question, since it is important to practicing pediatricians.

Dr. Jackson: In our experience the most common cause of low-grade fever, anorexia and elevated sedimentation rate has been infection of the sinuses. In addition many of these children are undernourished and chronically fatigued. The clinical course of the patient usually will rule out the diagnosis of rheumatic fever.

Chairman Hill: Dr. Harris, will you continue?

Dr. Harris: If I may put in a word in respect to the last question, I think that every pediatrician, for his own peace of mind, should periodically read an excellent paper by T. Duckett Jones, in the J.A.M.A. (1944), in which he lists 4 major signs of rheumatic fever without at least one of which he will not make a diagnosis of this disease. Dr. Hubbard has covered that ground.

Dr. Jackson: I would like to comment, if I may, in regard to Doctor Hubbard's discussion of migratory arthritis, I think it needs to be emphasized that in the younger child polyarthritis is not an outstanding clinical sign of rheumatic fever but rather carditis, while in the older patients migratory polyarthritis is common as well as other exudative manifestations of the disease and carditis is less severe.

Chairman Hill: Dr. Hubbard, do you want to comment on that?

Dr. Hubbard: That is the next question which I had before me. It has already been pretty well established that younger children are more apt than older children to have cardiac findings as the first manifestations of the disease rather than joint pains.

This question reads, however: "In younger children, are not joint pains minimal?"

In the individual child with acute polyarthritis or rheumatic origin, the joint pains may indeed not be minimal, but may be a very severe illness. But let that not confuse the fact that such cases are less apt to occur in the younger patients than in the older patients.

This same questioner also puts down on the note: "Erythema marginatum and sensitivity to sulfonamides."

It was brought out in one of the papers read to you that sulfonamides are not indicated in the treatment of active rheumatic infection. Since erythema marginatum occurs only with active infection there should be no chance of confusion.

The various skin manifestations of sulfonamide sensitivity are apt to be rather varied. The skin

manifestation of rheumatic fever, which we designate erythema marginatum, is a very characteristic picture, as shown to you in the lantern slide.

Chairman Hill: Dr. Jackson, would you care to answer that?

Dr. Jackson: It would be very useful if we could simplify this problem but, in my opinion, this is not possible with so many gaps in our knowledge. Migratory polyarthritis is a major manifestation of this disease especially in older children and adults. I only wanted to emphasize that the younger children may not have arthritis, but severe carditis, and if we centralize our attention on migratory arthritis the diagnosis in these patients may be delayed and treatment less effective.

Chairman Hill: Will Dr. Harris comment on that?

Dr. Harris: Since Dr. Jones' point was that at least one of those four basic criteria must be present, the significance of relative incidence of these major manifestations in the various age groups is as follows: In the younger patient, let us say, the dyspnea and carditis would be more noticeable in a higher percentage of cases, whereas in the older people the polyarthritis and the nodules would play a role in a relatively larger percentage of cases.

This useful rule is, therefore, not affected by the relative frequency of incidence of these major rheumatic manifestations in different age groups or in different sections of the country.

(The meeting adjourned.)

Pediatrics

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SPECIAL FEATURE SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

AN OPEN FORUM

EDWARDS A. PARK, M.D., *Editor,* PAUL HARPER, M.D., *Associate*

Statements appearing in this column do not necessarily reflect the opinion of the editors nor are they to be interpreted as the official opinion of the Academy.

INTRODUCTION

THE first two communications are the final ones dealing with school health programs. Dr. George M. Wheatley was Assistant Director of the Astoria Study of School Health, has served for many years on the Committee on School Health of the American Academy of Pediatrics, and is 3rd Vice-President of the Metropolitan Life Insurance Company. Dr. Harold H. Mitchell was Chairman of the Committee on School Health of the American Academy of Pediatrics from 1935 to 1948, and is currently Director of the School Health Program in Montgomery County, Maryland.

The letter from Dr. William J. Orr refers to his earlier communication published in this column, December 1948.

DEAR DR. HARPER:

You have asked me to give my ideas on the purposes of a school health program and suggestions on ways the physician can help to reach these objectives. I shall try to make them brief and to the point.

It seems to me that the school health program exists for the purpose of determining the health needs of school children and meeting these needs as effectively as possible. Such a program is therefore concerned with the school environment; health teaching and physical education, and medical, nursing and other health services.

1. Children need to live in a safe and healthful school environment which is conducive to good physical, mental and emotional growth. This includes such things as adequate ventilation, lighting, heating; sanitary food and water supplies; safe, well-kept and adequate play space in school buildings and grounds, and the creation and maintenance on the part of understanding adults of an atmosphere which accepts children as individuals with rights and privileges as well as responsibilities.

2. Children need to have opportunities to acquire on their own level of understanding the best available scientific knowledge concerning health and to have experiences in applying this information to their everyday living. This includes sound teaching on health habits, science, safety, physical education, social studies, home economics and other topics.

3. Children need to have careful health appraisals to determine their health status and to have access to the facilities necessary to prevent or care for any health disorder.

These three phases of the school health program are interrelated and their full development depends on the cooperative activity and interest of all school personnel. Each member of the school staff, parents and children, and community health workers contribute to a good school health program. When one activity is weak, all the others are affected.

The responsibility for the coordination of the various parts of the school health program is primarily that of the school administrator who relates health to the whole educational program. The classroom teacher, the school physician, the school nurse, the special teacher, the custodian and many others have their specific and continuous responsibilities to the school health program which the school administrator must define and develop in relation to the needs of his children. He depends on the school physician to participate in and contribute to the school health program in many ways even though the physician's particular concern is with the personal health guidance of the children. The school physician gives advice on the physical conditions in the school; he helps to see that facilities are used properly; he helps with the planning of the school program to provide for individual differences of students and teachers, and he determines way of providing necessary improvements. He supports the health and physical education program, giving professional advice on materials and activities, and encourages the integration of the health service program with the health education program.

The physician's prime responsibility is in the development and maintenance of a good health service program. Such a program has five fundamental elements.

1. *An adequate periodic medical examination and effective follow-up procedures:*

Determination of a child's health needs is a prerequisite to the proper functioning of the educational activities. Most school health services provide some kind of physical examination of the child, but in many places this is a very cursory inspection and does not adequately identify the child's health problems. Better results can be obtained by more careful but fewer examinations, including special consultation services and diagnostic laboratory services. Medical services in the schools often lack good pediatric supervision and direction. School physicians who usually are part-time general practitioners often do not have an understanding of growth and development in children. Consequently, many children have been labeled as endocrine cases or described as having flat feet or bad tonsils when these were perhaps slight deviations from the average growth pattern. School health examinations would be improved if more attention were paid to such things as the diet history, the amount of rest obtained, behavior characteristics, and symptoms of good or poor emotional health. Time would be saved, and a better definition of vision and eye defects obtained, if screening procedures were introduced to test for vision and hearing defects. The school health examination is a very expensive personal health service and to examine adequately every child every year under public auspices would be a prohibitive expense. Not only this but it is poor education because it does not encourage families who could afford their own physician to have this examination done by the family doctor or dentist. Also, children should learn that the family doctor and dentist are community rather than school services and are continually available. Better use of

these community resources would do away with the tendency to spread the limited school health services too thin, and would provide better opportunity for making health services in the school the educational experience which it ought to be for children.

2. *Parent participation and responsibility:*

Where real efforts to secure parent participation in school health activities have been made, they have often been successful, particularly in the elementary grades. The responsibility for the health of the child lies primarily with the family. The school physician, teacher and others, can learn a great deal from parents about the health history and individual needs of children and they in turn can help parents to understand the problems and to find ways of meeting them.

3. *Participation of teachers and other school personnel:*

When the knowledge and understanding of teachers and other members of the school staff about children's individual problems are used, the health services become more meaningful. At present the bulk of the physician's time is spent in routine examinations which does not permit him to do an adequate amount of consultative work. Teachers are anxious for help from the school physician to increase their knowledge and insight into child health needs and to make the teaching of health in the classroom more valuable. Other school personnel, such as administrators, custodians, nutritionists, and guidance workers, are equally anxious to benefit by the advice of physicians.

4. *Cooperation between the departments of health and education:*

Cooperation between the department of health and the department of education is a basic requirement for a good school health service. Fortunately, this is better appreciated today than it was a few years ago. Each department has an important contribution to make to the total program. On the one hand, the health department is the official legally constituted agency with responsibility for the health of the entire community. It has the technical personnel and the health knowledge which can and should be brought to bear on the school child's health. It is concerned with sanitation and communicable disease control, and in discharging these duties, the health department comes in contact with the school in every community. On the other hand, the education department is responsible for the supervision of children in its care throughout the school day. It is also responsible for their education, and today we are aware of the great importance of health education as a foundation for good personal health. Education departments may have a more adequate budget for school health work than health departments. The latter have been of more recent origin and have not been so well-supported with tax funds. The money necessary for the school health service represents a smaller item in the total education department budget than in the health department budget. In the latter department school health service is often the largest single item and when the health department has to reduce its expenses, it is likely to cut the school health service budget first because of its larger proportion. School health authorities are agreed that neither the health department nor education department can do the job of providing good school health services by themselves. Team work is required. In a number of states we now have interdepartmental committees or councils to bring the two departments together. Duplication of service is avoided, especially when the health department may be providing school health service to the parochial schools and the education department furnishing school health service to the public schools. These councils or committees have been very successful in bringing about better understanding between the two departments and in providing a more intelligent, as well as more efficient, school health program.

5. *Use of community resources:*

School health services would be improved if greater use were made of the existing community resources. This calls for considerable activity on the part of those responsible. Many conferences and meetings held with medical and dental authorities, with medical and dental societies, hospitals, safety organizations and other community resource directors often convince them of the importance of school health work and of the necessity of their active participation. If there are medical schools in the community, the assistance of the Pediatric Department may be obtained for in-service education of school personnel. This type of cooperative endeavor pays big dividends in creating a better understanding of what schools are trying to do and the problems they face, and, more important perhaps, in securing help for those children who need it.

SUMMARY

The keynote of a good school health program is cooperation. Effective working relationships among parents, school staff, and health personnel are essential. Continuous education on the growth and development problems of children and active participation on the part of all concerned with the health of children are basic.

A good school health program is a dynamic program. It is bent on determining the changing needs of many individuals and on meeting these needs in the most effective way possible with all the variety of physical facilities and human resources to be found in the school and community.

The pediatrician has a unique contribution to make in meeting the objectives of the school health program and in interpreting them to the community.

Sincerely yours,

(signed) GEORGE M. WHEATLEY, M.D.

DEAR DR. HARPER:

It seems very appropriate that the school health program should be discussed in THE PEDIATRICIAN AND THE PUBLIC because it may well be that no field of medical service offers more opportunity at this time to boost the public relations of the medical profession. Now that we are at last becoming so acutely aware of the need for considering public relations, I should like to try to express why I regard school health as so important.

We will bungle our public relations, indeed, if there is any confusion between our opposition to "compulsory health insurance" and our attitude towards "a 10 year program" for "The Nation's Health." We cannot afford to neglect those parts of a national program that we approve.

It helps very little to deny that we are "prejudiced." The really convincing evidence of the profession's concern for the public's interest, rather than for our personal or professional interest, is what we do about the many public health problems that we know most about. We can and have been very effective when we have joined hands with P.T.A.'s, health councils, and other citizen groups who sponsor the kind of public health programs that we approve. For example, we could demonstrate that we now know how to move forward rapidly on tuberculosis control, but the governmental appropriations have been putting economy before lives and control of the disease. The constructive proposals of the AMA, of various national, state and city medical societies provide plenty of scope for "a 10 year program" because we can demonstrate their effectiveness. These are the real antidotes for the unworkable proposals for bureaucratic control of medicine.

The School Health Program is such a constructive program and like public education is distinctly a part of our democratic society. But very few schools have more than a gesture to show for the public's support.

Here is a great opportunity to develop constructive policies in the schools that are needed as an essential part of a National Health Program. In recent years there has developed an increasing realization that medical advice is needed, and the job to be done must be a joint project of educators, public health workers and all the physicians who give service to children.

The first outstanding need is to correct the confusions as to what a physician can and cannot do, or should and should not spend his time at.

The second job is to stop the conflict over jurisdiction between the educators and the public health workers.

The American Academy of Pediatrics has consistently, since its founding, indicated its concern over these confusions and conflicts in school health programs. The reports of the Committee on School Health have had unwavering support from the Executive Board. We might even say that the Academy and the American Medical Association have consistently supported and promoted school health programs of a better and higher standard of quality for more and more children of this country. They have consistently pointed out the shortages and weaknesses of this service for American children.

It would certainly help many people, who are now confused by the controversy over "compulsory health insurance," to see that the profession is aggressive in the interest of the public welfare. It should make clear that the profession is concerned about having a better informed public on matters such as health protection, disease prevention and healthful living. It would emphasize the profession's interest in health education in the schools. It could prevent the extension of medical care as a part of the public school program. Indeed, the profession could see that the school service offers a type of medical guidance and education that does not conflict with private practice.

The part that the medical profession might play in correcting confusion and rivalry and in establishing a position of leadership has been very largely the subject of the reports of the Committee on School Health of the American Academy of Pediatrics. The more important reports of this Committee from 1935 to 1948 are listed at the end of this letter and are summarized, in so far as this is possible, in the following paragraphs.

Some Proposals of the Committee on School Health, 1935-1948

The Attempt To Do the Impossible

The school service should not pretend to give medical health supervision by routine medical examinations. Misrepresentation or misunderstanding of the limitations of the health examination service in schools leads to a false sense of security. When schools attempt to take over thorough and complete medical supervision, they lose their effectiveness as an educational force working towards an ideal. The overload of examinations is generally the most serious threat to an effective use of the physician's time in school.

A more effective plan for school examinations is proposed in the recent report of the Joint Committee of the American Medical Association and the National Education Association entitled "Health Appraisal of School Children." The use of the physician's time in the schools and standards for school medical examinations were presented in the Journal of Pediatrics for March, 1947. This Committee report also made pertinent suggestions

concerning the conditions which should determine the frequency of the school medical examinations and the procedures necessary for a more effective use of the physician's time.

The Part of the Teacher

All qualified health workers in the schools now appreciate that the day by day observations of the teacher are essential in order that significant disease and health disorders may be recognized early and guided in obtaining the medical attention needed. It has been demonstrated that regularly scheduled teacher-nurse conferences can contribute to the judgement of the teacher in selecting the children most likely to be in need of medical care.

State Laws and Policies Handicap Service

State laws in many states require routine medical examinations regardless of the budget available for employing physicians or for nurses to assist in follow-up. More and more examinations, about which nothing is ever done, create a defeatist attitude and nullify the educational and guidance purpose of the service. Mandatory annual examination laws should be amended and adequate budgets provided to make the service effective.

Evidence of Unmet Medical Needs Is Essential

A reasonably adequate medical and nursing staff should not only identify the children in need of medical attention, but also accumulate the evidence necessary to determine the adequacy of medical facilities for all socio-economic groups of school children. School records should show all cases of medical neglect. Records of the children who do not secure medical service because of limited income, or because of insufficient follow-up, or inadequate interpretation of the needs to the parents are the kind of evidence of adequacy or inadequacy of medical facilities that are needed for any system of medical practice. The school health program should also develop evidence concerning the follow-up staff needed to provide for the education and guidance necessary for a proper use of those facilities. Such records and facilities for maintaining records are an essential part of any program for a sound distribution of medical service.

An Organization Plan Needed

Whatever the source of income for meeting the needs of the school health program, both the Department of Health and of Education must accept the responsibility for the development of the facilities, the special staff and the use of the resources of the community for meeting the needs of children. The schools have an important part to play in education and guidance in the use of diagnostic and treatment facilities, even though the schools should not take over these facilities. The schools must also make use of properly interpreted medical information for the education, development, and adjustment of children with special needs. Case findings, teacher observation, and education for attitudes concerning medical care cannot be conducted without the help of the school authorities. Communicable disease control is not limited to the school and is primarily a health department function, but both departments must cooperate in the service. Health education for parents and service for preschool children is an essential part of the school health program.

Neither the health department nor the education department alone can do the whole job of meeting the health needs of children of school age. The only way that duplication

can be avoided and economical administration can be assured is through joint planning by both departments with the cooperation of the medical society in the plans for meeting medical needs.

Planning Requires a Medical Administration

The importance of medical advice in connection with a school health program unquestionably requires well-qualified medical personnel. "All personnel rendering health services must be properly supervised by qualified members of their own profession."* A medical administrator is therefore essential to obtain an economical and effective use of the physician's and nurse's time with a given budget.

Medical Education as a School Health Program Policy

The physician in the schools needs in-service training opportunities to learn the most effective techniques of personal guidance to persuade and educate parents and teachers in the health care and education of children. His work as a consultant and medical advisor offers such opportunities for learning preventive pediatrics and health education as cannot be achieved in an already overcrowded undergraduate medical curriculum. The common medical problems of children, such as nose and throat conditions, allergy, nutrition, endocrinology, rheumatic fever, and mental health, are particularly appropriate for postgraduate study, seminars and round table discussion and add interest and enthusiasm to school medicine.

Consultation services should be available and provision should be made for the physician in the schools to consult with a competent cardiologist, otologist, orthopedist, dentist, psychiatrist, dermatologist and ophthalmologist in cases selected for referral to these services. Seminars with such consultants provide opportunities for further information on the use of specialists in the care and supervision of children.

Young Physicians in the Schools

In-service education is essential for the staff of any wide-awake, continuing program, but that is not the most important reason for providing time and remuneration for round tables and seminars for the medical staff. The staff physician in the schools is most effective as a part time worker engaged in clinical practice. It is not a career job. The early years of building a practice are opportune for both the young physician and the school health program. The service provides both remuneration and learning opportunity to the physician when he has the time. The school health program benefits not only from the up-to-date knowledge, skills and enthusiasm of the young physicians from modern medical schools, hospitals and clinics, but most important of all the service benefits from a continuing influx of practitioners into the community who understand the fundamentals of the school health service and cooperate effectively with the school health program.

Probably one of the most serious handicaps in the follow-up of physical defects, guidance for the handicapped child, the health education of parents and children and the development of health examinations and medical supervision by the practitioner has been the lack of a liaison between the physician in the schools and the physician in private, prepaid or clinic practice. Understanding the school health service is probably

* Principles for Consideration in Judging the Probable Effectiveness of Federal Legislation Designed to Improve the Health of Children of School Age, PEDIATRICS: 1:569, 1948.

three-fourths of this problem. Occasional telephone conversations and an exchange of notes with the help of the nurse are usually sufficient liaison for the practicing physician who has had experience in a sound school health service.

To reach as large as possible a proportion of physicians in a community so that the profession can understand and cooperate effectively with principals, teachers and the school health staff, the employment policy for school physicians should provide:

1. Part-time employment for limited periods.
2. In-service training courses.
3. Reasonably generous remuneration to school physicians and to teachers for in-service training.

Professional Qualifications for School Physicians

The medical administrator should meet, in addition to basic pediatric training, standards of training and experience in public health administration and education.

Staff physicians should meet qualifications in terms of pediatric training in so far as qualified physicians are available. The Executive Board of the Academy recommended six grades of training and experience for all public services in child health starting with the first preference for "Specialist certified by the American Board of Pediatrics" and the sixth in preference suggested as "Part time specialty in pediatrics with pediatric appointment in registered hospital."

Résumé

1. The public wants a school health program as a part of the National Health Program.

2. The medical profession has consistently approved and supported plans for better school health programs.

3. A large job remains to provide sound school health programs.

4. Confusion as to policies and rivalry over jurisdiction provide an opportunity for medical leadership.

5. Certain proposals of the American Academy of Pediatrics suggest concepts important for the correction of the confusion and rivalry.

Sincerely yours,

(signed) HAROLD H. MITCHELL, M.D.

Reports of the Committee on School Health, 1935-1948

1. Forty years of school medical inspection, J. Pediat. **7**:714, 1935. (A critical historical review.)
2. Pediatric practice and school medical service, J. Pediat. **11**:140, 1937. (The response of 687 members of the Academy to questions concerning school medical service.)
3. Reports of state chairmen, Proceedings of the American Academy of Pediatrics, J. Pediat. **12**:838, 1938. (Comments on national organizations concerned with school health.)
4. Round table discussion on school health problems and relation to pediatrics, Proceedings of the American Academy of Pediatrics, J. Pediat. **14**:385, 1939.
5. Report of the Committee on School Health and School Health Education, J. Pediat. **19**:135, 1941.
6. Encouraging trends in school health, Report of the Committee on School Health of the Academy of Pediatrics, J. Pediat. **19**:721, 1941.
7. Discussion on how school may aid pediatrician, J. Pediat. **21**:686, 1942.
8. Medical standards for physicians in schools, J. Pediat. **21**:619, 1942.
9. Wheatley, G. M., Recent advances in school health service, J. Pediat. **24**:470, 1944.
10. Committee on School Health proposes broader objective for school medical service, J. Pediat. **29**:384, 1946.

11. Further comments on standards for school medical examinations, Report of the Committee on School Health, J. Pediat. **30**:343, 1947. (Discussion of frequency of examinations and use of the physician's time.)
12. Federal legislation for school health, PEDIATRICS **1**:102, 1948.
13. More on Federal legislation for school health, PEDIATRICS **1**:247, 1948.
14. Special report concerning two great weaknesses of school health programs: Rivalry over jurisdiction and treatment of children in need of medical attention, PEDIATRICS **1**:528, 1948.
15. Wegman, M. E., and Platou, R. V., in Pediatrician and Public, PEDIATRICS **2**:732, 1948. (The rivalry over jurisdiction becomes even more absurd.)
16. Rheumatic fever and school child, Special Report from the Committee on School Health and the Committee on Rheumatic Fever, PEDIATRICS **2**:321, 1948.

February 25, 1949

Dear Dr. Park:

It has been called to my attention that there is an inference in my recent communication to PEDIATRICS, which might be construed as an accusation against Dr. Thomas O. Gamble and accusing him of a falsehood.

I am extremely sorry if any inference was suggested in my communication. I only wished to quote from the minutes of the State Society with no thought of accusing Dr. Gamble of a falsehood.

Sincerely,

(signed) WILLIAM J. ORR, M.D.

TRENDS

IN HEALTH LEGISLATION AND ADMINISTRATION

By JOHN P. HUBBARD, M.D., *Contributing Editor*

This and subsequent descriptions of events and trends are intended to be unbiased and factual, presenting both sides of controversial matters so that conclusions may be formed from critical appraisal of things as they are. These statements do not necessarily reflect the opinion of the writer nor are they to be interpreted as official opinion of the Academy.

ON March 21 the Hoover Commission's final report on the reorganization of the Government's medical and hospital services was submitted to the Congress. The report prepared by the bi-partisan12-man Commission is not in accord with the proposal to create a cabinet department of welfare which would include the present functions of the Federal Security Agency—a proposal which is incorporated into a House bill (H. R. 782) and, as stated in this column a month ago, has been approved by the House Committee to which it was referred. In contrast to H. R. 782, the Hoover Commission recommends a new cabinet department to direct the welfare and educational program of the Federal Government and a new and separate United Medical Administration. The UMA would be responsible directly to the President and should, according to the Commission, be headed by "the ablest medical and health administrator whose services can be obtained by the government," with three assistant administrators and an advisory board composed exclusively of Federal officials. It is noteworthy that the qualifications recommended for the person who should head the UMA does not specify that he should be a doctor of medicine.

The cabinet department, for which no name has as yet been proposed, would have jurisdiction over the Bureau of Old Age and Survivor's Insurance, the Bureau of Public Assistance, the Children's Bureau, the Bureau of Education, the Bureau of Vocational Rehabilitation, the American Printing House for the Blind, the Columbia Institution for the Deaf and the Bureau of Indian Affairs.

Note that the Commission recommends that the Children's Bureau be included in the new cabinet department whereas the U. S. Public Health Service and all of the other Government's major services in the fields of medical care, public health and research would be transferred to the new UMA.

The UMA would consolidate under civilian control the Army, Navy, Air Force and Veterans Administration hospitals along with the Marine hospitals now operated by the USPHS. The Veterans Administration would be stripped of all its hospitals and the Military of all except three, one each for Army, Navy, and Air Force.

Other recommendations of the Commission included Federal aid to medical education, starting with an immediate short range survey to be followed by a long range study; high priority to medical research; and constant attention to medical national defense.

As might well be expected, the recommendation of the Hoover Commission made prominent news the following day. We quote from the *New York Times,* March 22nd:

> The Commission conceded that its majority report had departed from the premise first given to its medical task force, namely that "the commission will recommend a cabinet department embracing health, education and security."
>
> Vigorous criticism of the proposed new medical setup is expected from several sources. The program, which would take away from the armed forces and the Veterans Administration their

national network of hospital facilities, already has been condemned by the American Legion and the Veterans of Foreign Wars.

Dean Acheson, Secretary of State and vice chairman of the commission, was joined by Senator George D. Aiken, Republican of Vermont, and James H. Rowe, Jr., a former administrative assistant of President Roosevelt, in a strong minority dissent. They described the proposal to establish a new medical agency as "unsound organization and unnecessary governmental structure."

Commissioner James Forrestal, retiring Secretary of Defense, abstained from voting on the medical proposal because of his official position. Mr. Hoover was one of those who favored the proposal. Representative Clarence J. Brown, Republican, of Ohio, also dissented on the matter. He defended the present military hospital system.

The minority report contended that to take the Public Health Service out of the Federal Security Agency and put it into a new medical administration would "serve only to splinter the Government's welfare functions" and "cause more of the organization confusion which this commission was created to terminate."

If the commission's proposal to create a new department to handle welfare and educational activities is adopted by Congress it is considered probable that Oscar R. Ewing, Federal Security Administrator and friend of President Truman, would get the Cabinet post.

The commission suggested that the staff of the new department should comprise a secretary, an undersecretary and three assistant secretaries, one of whom should be administrative assistant secretary in charge of staff services.

There was no disagreement among the commission members relative to the proposed new department. Messrs. Acheson, Aiken and Rowe dissented on the separation of the health functions from other welfare activities, however. . . .

Mr. Hoover explained his own deviation from the original idea of putting the proposed new health organization in a Department of Welfare. In a supplemental report of dissent on advisory board powers, he was joined by Commissioner Carter Manasco.

They recommended the creation of an advisory board on policy that would work with the medical administrator of the new health organization. It would consist of the Surgeons General of Army, Navy, Air Force, Veterans Administration and Public Health Service.

"It has been suggested," Messrs. Hoover and Manasco said in their report, "that the new organization should be placed in a Department of Welfare. Under ordinary circumstances we would agree with this proposition, but we think that it is imperative that the board proposed by us have policy-making power. We do not think that a Cabinet officer should be placed in the embarrassing position of having an agency under him without the control of policy."

JOSEPH S. WALL, M.D., *Chairman*
Committee on Legislation

PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

LEONA BAUMGARTNER, M.D., *Contributing Editor*

INFANT AND CHILDHOOD MORTALITY: 1947

THE infant mortality rate in 1947 was the lowest on record, according to figures released by the National Office of Vital Statistics of the Public Health Service, Federal Security Agency. The number of deaths under one year recorded in the United States during 1947 was 119,173, or 8,110 more than the number (111,063) reported in 1946. However, this increase reflects the tremendous increase in the number of births during 1947 and not a rise in infant mortality. The relative frequency of infant deaths as

TABLE 1

DEATHS UNDER 1 YEAR AND INFANT MORTALITY RATES, BY AGE, RACE, AND SEX: UNITED STATES, 1947
(Exclusive of stillbirths. Rates per 1,000 live births)

Age	Total	Race		Sex	
		White	Nonwhite	Male	Female
			Number		
Under 1 year	119,173	98,547	20,626	68,622	50,551
Under 1 day	39,716	33,956	5,760	23,064	16,652
1 day	12,683	10,979	1,704	7,490	5,193
2 days	7,890	6,808	1,082	4,781	3,109
3–6 days	10,996	9,013	1,983	6,471	4,525
7–13 days	6,173	4,859	1,314	3,509	2,664
14–20 days	3,600	2,922	678	1,975	1,625
21–29 days	3,238	2,575	663	1,852	1,386
Under 1 month	84,296	71,112	13,184	49,142	35,154
1 month	7,528	5,899	1,629	4,371	3,157
2 months	5,971	4,702	1,269	3,391	2,580
3–5 months	11,211	8,838	2,373	6,226	4,985
6–8 months	6,367	4,977	1,390	3,430	2,937
9–11 months	3,800	3,019	781	2,062	1,738
			Rate		
Under 1 year	32.2	30.1	48.5	36.1	28.1
Under 1 day	10.7	10.4	13.5	12.1	9.3
1 day	3.4	3.4	4.0	3.9	2.9
2 days	2.1	2.1	2.5	2.5	1.7
3–6 days	3.0	2.8	4.7	3.4	2.5
7–13 days	1.7	1.5	3.1	1.8	1.5
14–20 days	1.0	0.9	1.6	1.0	0.9
21–29 days	0.9	0.8	1.6	1.0	0.8
Under 1 month	22.8	21.7	31.0	25.9	19.5
1 month	2.0	1.8	3.8	2.3	1.8
2 months	1.6	1.4	3.0	1.8	1.4
3–5 months	3.0	2.7	5.6	3.3	2.8
6–8 months	1.7	1.5	3.3	1.8	1.6
9–11 months	1.0	0.9	1.8	1.1	1.0

TABLE 2

DEATHS UNDER 1 YEAR AND INFANT MORTALITY RATES FOR SELECTED CAUSES: UNITED STATES, 1946 AND 1947
(Exclusive of stillbirths. Rates per 1,000 live births)

Cause of Death	Number		Rate	
	1947	1946	1947	1946
ALL CAUSES	119,173	111,063	32.2	33.8
Cerebrospinal (meningococcus) meningitis	281	270	0.1	0.1
Scarlet fever	8	6	0.0	0.0
Whooping cough	1,481	869	0.4	0.3
Diphtheria	58	84	0.0	0.0
Tuberculosis (all forms)	370	406	0.1	0.1
Tuberculosis of the respiratory system	146	182	0.0	0.1
Tuberculosis of the meninges	124	126	0.0	0.0
Tuberculosis (other forms)	100	98	0.0	0.0
Dysentery	423	480	0.1	0.1
Malaria	9	12	0.0	0.0
Syphilis	517	538	0.1	0.2
Measles	116	297	0.0	0.1
Diseases of the thymus gland	929	934	0.3	0.3
Meningitis (not due to meningococcus)	669	506	0.2	0.2
Intracranial lesions of vascular origin	182	140	0.0	0.0
Convulsions	204	256	0.1	0.1
Diseases of the ear and mastoid process	174	169	0.0	0.1
Diseases of the heart	161	156	0.0	0.0
Pneumonia (all forms) and influenza	13,198	12,657	3.6	3.8
Bronchopneumonia	7,999	7,502	2.2	2.3
Lobar pneumonia	2,239	2,187	0.6	0.7
Pneumonia (unspecified)	1,895	1,725	0.5	0.5
Influenza	1,065	1,243	0.3	0.4
Other diseases of the respiratory system	1,152	901	0.3	0.3
Ulcer of the stomach or duodenum	36	26	0.0	0.0
Diarrhea, enteritis and ulceration of the intestines	5,590	5,498	1.5	1.7
Intestinal obstruction	559	441	0.2	0.1
Other diseases of the digestive system	554	483	0.1	0.1
Nephritis	100	106	0.0	0.0
Congenital malformations	17,076	14,912	4.6	4.5
Diseases peculiar to first year of life	65,308	61,738	17.7	18.8
Congenital debility	1,718	1,797	0.5	0.5
Premature birth	41,053	39,824	11.1	12.1
Injury at birth	13,075	11,738	3.5	3.6
Other diseases peculiar to first year of life	9,462	8,379	2.6	2.5
Asphyxia and atelectasis	5,756	4,825	1.6	1.5
Infection of the umbilicus and other specified diseases	3,706	3,554	1.0	1.1
Homicide	174	134	0.0	0.0
Accidental deaths	3,557	2,915	1.0	0.9
Accidental mechanical suffocation	1,663	1,344	0.4	0.4
Other accidental deaths	1,894	1,571	0.5	0.5
Ill-defined and unknown causes	4,095	4,129	1.1	1.3
All other causes	2,192	2,000	0.6	0.6

TABLE 3

DEATHS UNDER 1 YEAR AND INFANT MORTALITY RATES: UNITED STATES AND EACH STATE, 1946 AND 1947

(By place of residence of the mother of the child. Exclusive of stillbirths. Rates per 1,000 live births)

Area	Number		Rate	
	1947	1946	1947	1946
United States	119,173	111,063	32.2	33.8
Alabama	3,301	3,025	37.5	37.9
Arizona	973	679	50.8	41.5
Arkansas	1,445	1,283	29.5	28.3
California	7,233	6,705	29.4	30.7
Colorado	1,234	1,180	37.5	40.0
Connecticut	1,150	1,154	25.2	27.8
Delaware	239	202	31.0	29.7
District of Columbia	691	767	31.9	41.2
Florida	2,285	2,116	38.2	39.4
Georgia	3,251	3,075	34.2	35.9
Idaho	478	453	29.4	32.9
Illinois	5,672	5,316	28.9	30.4
Indiana	2,949	2,697	30.6	31.5
Iowa	1,817	1,681	28.5	29.9
Kansas	1,251	1,217	28.1	30.6
Kentucky	2,971	2,900	37.1	40.0
Louisiana	2,773	2,553	37.2	37.2
Maine	853	833	35.7	41.0
Maryland	1,794	1,713	31.6	34.0
Massachusetts	3,027	2,984	28.1	31.6
Michigan	5,080	4,552	31.5	32.7
Minnesota	2,165	1,925	28.6	28.6
Mississippi	2,448	2,311	36.8	37.5
Missouri	2,929	2,665	32.5	33.0
Montana	484	448	32.1	34.8
Nebraska	894	846	27.8	30.2
Nevada	134	130	33.2	39.6
New Hampshire	399	348	30.1	31.4
New Jersey	2,965	2,715	27.9	28.5
New Mexico	1,379	1,415	67.9	78.2
New York	9,123	8,345	28.2	29.1
North Carolina	3,938	3,742	34.9	37.2
North Dakota	523	519	30.6	34.0
Ohio	5,817	5,312	29.5	31.3
Oklahoma	1,733	1,639	32.3	32.5
Oregon	895	833	24.7	27.7
Pennsylvania	7,741	7,196	31.1	33.0
Rhode Island	522	494	28.2	29.5
South Carolina	2,352	2,235	39.5	41.4
South Dakota	511	432	30.9	29.6
Tennessee	3,144	2,974	36.3	38.5
Texas	8,161	7,564	41.1	41.7
Utah	545	496	25.1	27.2
Vermont	303	284	31.2	34.0
Virginia	3,142	2,935	36.6	38.7
Washington	1,643	1,734	28.1	33.4
West Virginia	2,091	1,990	38.0	40.9
Wisconsin	2,476	2,246	29.5	30.0
Wyoming	249	205	34.0	33.1

measured by the infant mortality rate decreased from 33.8 per 1,000 live births in 1946 to 32.2 in 1947. Provisional figures indicate a further decline in 1948 to an estimated rate of 31.8.

The five leading causes of infant deaths in 1947 and the infant mortality rates for each are: premature birth, 11.1; congenital malformations, 4.6; pneumonia and influenza, 3.6; injury at birth, 3.5; and asphyxia and atelectasis, 1.6. These leading causes accounted for 75.7% of all the infant deaths in 1947. This was the first year that asphyxia and atelectasis ranked among the five leading causes of infant deaths and that diarrhea, enteritis and ulceration of the intestines has not been in this group. The number of deaths

TABLE 4

DEATH RATES BY AGE, RACE, AND SEX, UNITED STATES 1947 (TENTATIVE)

Age	All Races			White			Nonwhite		
	Both Sexes	Male	Female	Both Sexes	Male	Female	Both Sexes	Male	Female
All Ages*	10.1	11.5	8.7	9.9	11.4	8.5	11.3	12.5	10.2
1–4 years	1.6	1.7	1.4	1.5	1.6	1.3	2.5	2.6	2.3
5–9 years	0.7	0.8	0.6	0.7	0.8	0.5	0.9	1.0	0.8
10–14 years	0.7	0.8	0.5	0.6	0.8	0.5	1.1	1.2	1.0
15–19 years	1.3	1.6	1.0	1.1	1.4	0.8	2.4	2.6	2.3

* Includes deaths for which age was not stated.

under one year and infant mortality rates for selected causes in the United States during 1946 and 1947 are presented in Table 2.

The relative frequency of deaths under one year is greatest for the under one day age group and decreases steadily with age. Mortality is higher among nonwhite than white infants and among male than female infants. The number of infant deaths and infant mortality rates in the United States for 1947 by subdivisions of the first year of life, race, and sex, are shown in Table 1.

Table 3 presents the number of deaths under one year and infant mortality rates for the United States and each state in 1946 and 1947. The 1947 rates for the individual states ranged from 24.7 for Oregon to 50.8 for Arizona and 67.9 for New Mexico. To some extent, differences in state rates may be the result of variation among states in the completeness of both birth and death registration.

As in the country as a whole, the infant mortality rates for most of the states and for the District of Columbia were lower in 1947 than in 1946. In comparing state rates for 1946 and 1947 consideration must be given to the fact that the rates for some states are based on relatively small frequencies. In such instances a small difference in the number of infant deaths may result in a relatively large change in the rate without necessarily indicating a true change in infant mortality.

The National Office of Vital Statistics has also released tentative figures for deaths by age for the year 1947, for all groups in the population. The average age of death was 3.6 years higher for women than for men. The average (median) age of death for women was 66.9 years as compared with 63.3 for men. The other figures of particular interest to pediatricians are shown in Table 4.

Births Remain High in 1948

The second largest number of births in the history of this country occurred during 1948, according to data just released by the National Office of Vital Statistics of the Public Health Service.

The number of live births registered during 1948 was estimated at 3,559,000 or only about 4% below the all-time high of 3,699,940 for 1947. Of even greater significance are the figures which take into consideration the unregistered births. The total number of births (registered and unregistered combined) was estimated at 3,715,000 for 1948

TABLE 5

Number of Births and Birth Rates, by Month: United States, 1946–48
(Exclusive of stillbirths. Rates on an annual basis per 1,000 estimated midyear population)

Month	1948[1]		1947		1946	
	Number	Rate[2]	Number	Rate[2]	Number	Rate[3]
All months	3,559,000	24.4	3,699,940	25.8	3,288,672	23.3
January	291,000	23.5	340,460	28.0	222,721	18.6
February	279,000	24.1	301,932	27.4	206,387	19.0
March	299,000	24.1	325,740	26.7	228,321	19.0
April	280,000	23.4	292,375	24.8	220,646	19.0
May	274,000	22.1	303,461	24.9	233,452	19.5
June	272,000	22.7	301,913	25.6	242,302	20.9
July	309,000	25.0	318,340	26.1	286,336	23.9
August	319,000	25.8	319,681	26.2	312,678	26.1
September	320,000	26.7	310,145	26.3	325,485	28.0
October	315,000	25.5	308,540	25.3	339,499	28.3
November	295,000	24.7	288,366	24.5	332,115	28.6
December	306,000	24.7	288,987	23.7	338,730	28.2

[1] Estimated.

[2] Based on population excluding armed forces overseas. The armed forces overseas were 0.4% of the total population in 1947, and 0.3% in 1948.

[3] Based on population including armed forces overseas.

and 3,876,000 for 1947. Only eight years earlier, in 1940, the last pre-war year, the figure was little more than 2½ million (2,558,000).

The 1948 estimated birth rate of 24.4 per 1,000 population was about 5% below the final rate of 25.8 for 1947, but exceeded the 1946 rate (23.3) by almost 5%. (These rates and all other figures which follow are based on registered births.)

The striking changes that have occurred in the birth rate during the post-war period 1946-48 are more clearly shown in Table 5. Demobilization beginning in the last half of 1945 was reflected by extraordinarily high birth rates in the latter part of 1946. In 1947 the monthly rate declined from the peak rates experienced at the end of 1946 but was nevertheless at a high level throughout the year. The rates in the last half of 1948 were significantly higher than in the earlier months and about equalled the rates in the last half of 1947.

Final 1947 birth rates on a residence basis are now available for each state and the District of Columbia (Table 6). The state rates ranged from a high of 37.2 (per 1,000 population present in area) for New Mexico to a low of 22.8 for New York. The birth

TABLE 6

NUMBER OF BIRTHS AND BIRTH RATES: UNITED STATES AND EACH STATE, 1940 AND 1947
(By place of residence. Exclusive of stillbirths. Rates per 1,000 estimated midyear population)

Area	Number		Rate		
	1947	1940	1947[1]	1940[2]	Percent increase 1940 to 1947[3]
United States	3,699,940	2,360,399	25.8	17.9	44.1
Alabama	88,116	62,938	31.1	22.3	39.5
Arizona	19,153	11,503	29.7	22.8	30.3
Arkansas	48,983	38,473	25.6	19.7	29.9
California	245,889	112,287	25.1	16.2	54.9
Colorado	32,874	21,034	28.7	18.6	54.0
Connecticut	45,581	25,548	23.1	15.0	54.0
Delaware	7,717	4,551	26.5	17.0	55.9
District of Columbia	21,686	11,228	25.2	16.7	50.9
Florida	59,807	33,799	25.7	17.8	44.4
Georgia	94,944	64,757	30.3	21.0	44.3
Idaho	16,265	11,789	31.0	23.3	39.0
Illinois	196,007	124,615	23.3	15.8	47.5
Indiana	96,359	61,660	25.1	18.0	39.4
Iowa	63,858	44,854	24.6	17.7	39.0
Kansas	44,535	28,885	23.1	16.1	43.5
Kentucky	79,987	63,768	28.8	22.4	28.6
Louisiana	74,630	50,848	29.3	21.5	36.3
Maine	23,873	15,222	27.0	18.0	50.0
Maryland	56,687	32,365	26.5	17.8	48.9
Massachusetts	107,791	65,551	23.3	15.2	53.3
Michigan	161,085	99,021	26.5	18.8	41.0
Minnesota	75,577	52,915	26.2	18.9	38.6
Mississippi	66,450	52,732	31.7	24.2	31.0
Missouri	90,060	61,479	23.1	16.2	42.6
Montana	15,086	11,556	30.9	20.6	50.0
Nebraska	32,132	22,029	25.0	16.8	48.8
Nevada	4,041	2,109	29.1	18.8	54.8
New Hampshire	13,267	8,329	24.8	17.0	45.9
New Jersey	106,242	59,814	23.0	14.4	59.7
New Mexico	20,322	14,792	37.2	27.6	34.8
New York	323,250	196,088	22.8	14.6	56.2
North Carolina	112,877	80,455	30.5	22.5	35.6
North Dakota	17,064	13,135	31.5	20.6	52.9
Ohio	197,311	114,663	25.7	16.6	54.8
Oklahoma	53,684	44,887	23.5	19.4	21.1
Oregon	36,294	17,623	23.5	16.0	46.9
Pennsylvania	248,513	165,456	23.6	16.7	41.3
Rhode Island	18,536	10,830	24.9	15.3	62.7
South Carolina	59,470	44,612	30.5	23.7	28.7
South Dakota	16,539	12,054	28.6	18.9	51.3
Tennessee	86,619	55,242	28.0	18.8	48.9
Texas	198,662	127,072	28.0	19.8	41.4
Utah	21,724	13,347	33.9	24.1	40.7
Vermont	9,708	6,942	26.5	19.4	36.6
Virginia	85,740	57,014	28.6	21.2	34.9
Washington	58,481	28,159	24.8	16.2	53.1
West Virginia	55,085	42,289	29.3	22.1	32.6
Wisconsin	84,059	54,891	25.9	17.5	48.0
Wyoming	7,320	5,189	27.6	20.7	33.3

[1] Based on total population present in area.

[2] For the United States, based on total population including armed forces overseas; for the states, based on civilian population in area.

[3] Change in population base between 1940 and 1947 has only a minor effect on the comparison of rates in these two years. In 1947 armed forces overseas were 0.4% of total population and armed forces stationed in 47 states were less than 2% of the population present in the area.

rate for half of the states and the District of Columbia fell within the range 25.0 to 30.0. The rates for 14 states were below 25.0, while in 10 states they exceeded 30.0.

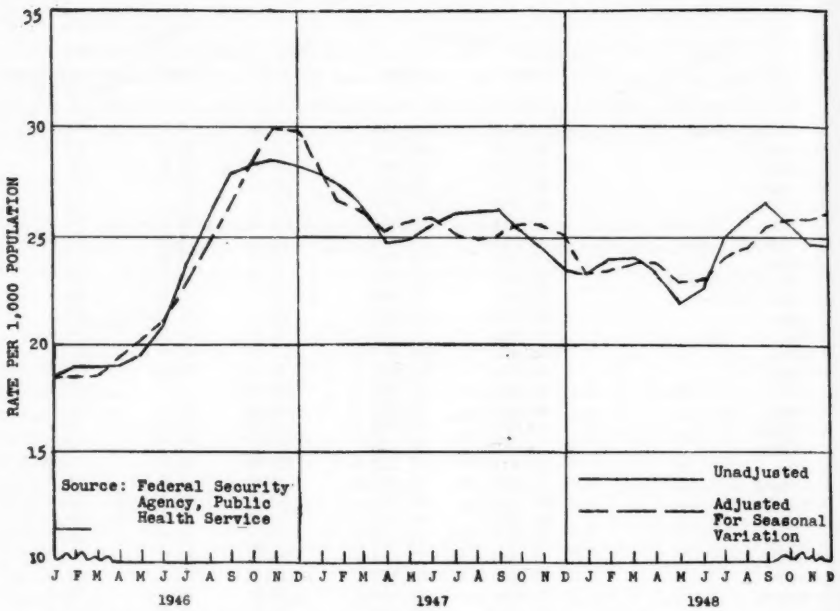
35
30
25
20
15
10
RATE PER 1,000 POPULATION
Source: Federal Security Agency, Public Health Service
Unadjusted
Adjusted For Seasonal Variation
J F M A M J J A S O N D J F M A M J J A S O N D J F M A M J J A S O N D
1946
1947
1948

CHART 1

Monthly Birth Rates (on an annual basis), Unadjusted and Adjusted for Seasonal Variation: United States, 1946-48.

The proportionate changes in the birth rates for each state between the last pre-war year, 1940, and 1947 are pictured in Chart 1 above. Fifteen states had increases of 50% or more; 15 increases of between 40 and 50%; 14 between 30 and 40%, and 4 between 20 and 30%. Greater proportionate increases were recorded in those areas which for many years have consistently had comparatively low birth rates.

INTERNATIONAL NEWS AND REPORTS

NEWS FROM ENGLAND

ALAN MONCRIEFF, *Corresponding Editor*

UNIVERSITY OF LEEDS: DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

A lecturer in Diseases of Children was first appointed in 1921 and later given the status of part-time professor in 1927. Some 19 years later (1946) the part-time chair in Diseases of Children was replaced by a whole-time chair in Pediatrics and Child Health. The formation of a university department began with the establishment of a whole-time chair. Departmental staff, other than secretarial, consists of the professorial head, his deputy, who has the status of lecturer, and three tutors. Of the tutors, one holds a resident appointment in a maternity hospital.

The rate and character of development has been conditioned by the stringency of post-war finances, by the claims of numerous competitive interests, and by the nature of clinical facilities available. Clinical facilities are limited in that there is a serious shortage of hospital beds in the city and that facilities for the hospital care of sick children are especially inadequate. There is no general hospital for children. While there is a residential "special school" for orthopedic patients there are no comparable provisions for convalescent or long-stay medical cases. For clinical material the university department is dependent upon wards in general hospitals, the policy of which is largely determined by the needs of adult patients. Not all beds in the medical wards for children are under the care of pediatricians. Inevitably, the disadvantages consequent upon these arrangements limit the value of the training provided for medical and nursing students, and restrict opportunities for research work. In contrast, provisions for study of the newborn are rather better, although carried out under difficult conditions. Arrangements exist for close cooperation with the city school health and infant welfare services, and valuable relations have been established with representatives of the family doctor and of voluntary organizations concerned with different aspects of the care of child life.

Teaching activities are concerned primarily with undergraduate training. Instruction given is planned to enable the newly qualified doctor to supervise the care of healthy and ailing children under conditions of family practice. The student is introduced to health and disease in infancy as found among the newborn babies in maternity nurseries. Thereafter, he studies child health in residential homes, and at infant welfare and school health clinics, and physical and mental ailments in the children's wards of general hospitals. Instruction given in the hospital outpatients department focusses attention on the mother-child relationship. The factor of home background is further emphasized by enabling students to visit the homes of some of the children who have been allocated to them for the purposes of "clerking".

In the training of the student equal attention is paid to the physical and emotional needs of the child. Visits are arranged to day "special schools" for children suffering from various forms of physical and mental handicap. Arbitrary differentiation of curative from preventive pediatrics is discouraged. Study of the individual child is considered in relation to social factors concerning the family, and to epidemiologic factors related to communities of children. To remind him of the gulf separating conditions under which he is taught from those under which he will practice the care of child health, the student is given an opportunity to attend a family doctor's afternoon surgery reserved for mothers and children. The arrangement is still in an experimental stage but promises to bring a certain realism, not otherwise possible, into the training of future family doctors in the care of child health.

The University Department of Pediatrics makes separate provision for the post-graduate instruction of medical officers in the employ of the city of Leeds child health services. These medical officers regularly attend hospital ward rounds and outpatients sessions, and together with the city midwives, health visitors and school nurses, take part in lecture-discussions specially arranged for them on selected aspects of child health. Other post-graduate instruction provided by the department includes demonstrations and week-end courses designed for family doctors, and a short course of lectures for practitioners studying for a diploma in public health.

Additional to instruction given the medical student, the Department contributes to separate University courses organised for sister tutors, teachers of midwives, health visitors, pupil midwives and

boarding-out officers. The view has been expressed that a university should not accept responsibility for instructional courses of this type. In the contributor's opinion, it is in the interest of child health that a university should undertake the responsibility. Certainly in so far as the University of Leeds is concerned, the policy gives the Department of Pediatrics and Child Health an opportunity to foster a common approach to the subject of child health among a variety of students, all of whom will, in one way or another, ultimately be concerned with the care of child life. This wide conception of child health has led to an association of interests with such other university departments as those concerned with the basic sciences, general medicine, public health, dental health, social science and education. As yet there is no comparable intermingling of medical and surgical interests concerned with child health. A problem confronting the department is that of promoting a satisfying balance as between curative and preventive concepts of child life and health. If present trends persist and if hospital facilities continue to be inadequate preventive care may receive disproportionate attention in teaching, to the detriment of instruction given in curative care. Departmental policy aims at encouraging that appreciation of the subject of pediatrics and child health which is necessary for effective academic instruction and for the successful advancement of child health on the field.

W. S. Craig, M.D.-F.R.C. P.Ed.

NEWS AND ANNOUNCEMENTS

The Metropolitan Life Insurance Company of New York, through Dr. George M. Wheatley, 3rd Vice-president in charge of Health and Welfare Services, has made possible distribution of reprints from the Company's "Statistical Bulletin" of memoranda of pediatric interest. The information is assembled from many sources and is not available in that form anywhere else. Fellows of the Academy will receive copies from the office of the Secretary. Copies also are available by writing to the Company, The Metropolitan Life Insurance Company, 1 Madison Avenue, New York City 10, N.Y., as long as the supply lasts. A recent publication of unusual interest is "Cancer Among Children," January 1949, Volume 3, No. 1.

* * *

Dr. James H. McKee, pediatrician and former Army flight Surgeon, died March 24, at the age of 78.

In 1918 Dr. McKee was one of the first to fly from coast to coast, making the flight with an Army squadron commanded by Gen. H. H. Arnold, former chief of the Air Forces, who then was Colonel Arnold. During the first World War Dr. McKee served as a major in the medical corps.

An alumnus of the Medical School of the University of Pennsylvania, he received a certificate from the Pennsylvania Medical Society in 1943 in recognition of his 50 years of service in his profession.

* * *

Dr. Rustin McIntosh, New York City, has been made chairman of the Council on Rheumatic Fever of the American Heart Association for 1949. He succeeds Dr. Harold M. Marvin.

* * *

St. Francis Sanatorium for Cardiac Children, Roslyn, L.I., N.Y., announces a Comprehensive Postgraduate Course in Rheumatic Fever and Rheumatic Heart Disease, at the Sanatorium, June 1 to June 14, 1949 (inclusive). Fee for course, $75.

This course is designed to give intensive training in the diagnosis and treatment of rheumatic fever and rheumatic heart disease.

For further information, address Rev. Mother Superior, F.M.M., Supt., St. Francis Sanatorium for Cardiac Children, Roslyn, L.I., N.Y.

* * *

Memorial Hospital Center for Cancer and Allied Diseases, New York, N.Y. has established a residency in Pediatrics.

The period of service is for a minimum of 6 months and its purpose is to train the pediatrician in the diagnosis and management of neoplastic diseases in childhood. The resident will also participate in the research program in progress at the Sloan-Kettering Institute. Three months' credit toward pediatric residency training requirements has been approved by the American Board of Pediatrics.

For further particulars applicants may communicate with the Director, Pediatric Service, Memorial Hospital Center for Cancer and Allied Diseases, 444 East 68th Street, New York 21, N.Y.

ERRATUM

In the December 1948 issue, volume 2, number 6, page 703, the first line of the third paragraph should read: "The clinical results from the other agents were unsatisfactory in that no cures or satisfactory remissions were observed," instead of "The clinical results from the other agents were satisfactory in that no cures or satisfactory remissions were observed."

In the February 1948 issue, volume 3, number 2, page 275, line 28 should read: "One to two drops of 1:10,000 solution of atropine, 0.01 to 0.02 mg./kg., represents the smallest effective dose," instead of "One to two drops of a 1:10,000 solution of atropine, 0.01 to 0.22 mg./kg., represents the smallest effective dose."

In the February 1949 issue, volume 3, number 2, on page 226 the electrocardiogram in Figure 3B is printed incorrectly. Lead I is printed upside down as Lead III; Lead II is printed upside down; Lead III is printed right side up as Lead I.

BOOK REVIEWS

MEDICAL WRITING, Morris Fishbein, M.D., ed. 2, $4.00, 265 pages, The Blakiston Company, Philadelphia, Pa., 1948.

The appearance of this addition is most welcome. It is hard to conceive of a writing style changing in a period so short as 10 years, but it does. The new words in use are an enormous number and there is a tendency to anglicize and shorten wherever possible. This book is the one authoritative source in the field of medical writing and has the backing of all attempts to organize and standardize the technic, if not the art, of writing. The latter is the more difficult to cultivate and attain. It is certain that if this book were adhered to fully, medical writing would be less prolific, more readable and because of its improved style would be more apt to carry a clear story of what is in the writer's mind. Every manuscript to be spoken or read should be subjected to a critical analysis, according to the standards set up in this book.

HUGH MCCULLOCH

YEAR BOOK OF PEDIATRICS, Henry G. Poncher, M.D., $4.50, 525 pages, Year Book Publishers, Inc., 304 S. Dearborn Street, Chicago 4, Illinois, 1948.

The 1948 edition of this popular Year Book marks a change of editorship to Dr. Poncher who is professor and head of the Department of Pediatrics, University of Illinois, College of Medicine, and who succeeds Dr. Isaac Abt. There is no major change in form or style and the book under its new editor should continue its popularity and usefulness. The editor states that the book is directed chiefly to readers who are general practitioners, as well as to practicing pediatricians. Articles which broaden a reader's perspective and give a sound foundation in physiology and pathology on which to base careful diagnostic reasoning and rational treatment are included. The plan of this Year Book in every way supplements others published as reviews of special subjects or complete indices of the literature. The publishers are to be congratulated on having obtained an editor so well qualified to follow in the footsteps of "the great master."

HUGH MCCULLOCH

PSYCHOPATHOLOGY AND EDUCATION OF THE BRAIN-INJURED CHILD, Alfred A. Strauss and Laura E. Lehtinen, Grune and Stratton, New York, 1947.

As the title indicates this book is divided into two parts: the psychopathologic and educational aspects of brain-injury in children. The following is the definition of the brain-injured or exogenous child given by the authors: "A brain-injured child is a child who before, during, or after birth has received an injury to or suffered an infection of the brain. As a result of such organic impairment defects of the neuromotor system may be present or absent; however, such a child may show disturbances in perception, thinking, and emotional behavior, either separately or in combination. These disturbances can be demonstrated by specific tests. These disturbances prevent or impede a normal learning process. Special educational methods have been devised to remedy these specific handicaps."

The psychologic studies conducted by Strauss and colleagues at the Wayne County Training Center are brought together for the first time here. These studies, in which exogenous and endogenous (familial or garden-variety) defectives are compared to each other, are presented to illustrate how the former differ from the latter in the spheres of perception, thinking, and behavior. For example, it was found that in a task requiring the individual to reproduce a design from a model, as in the marble board test, the reproductions of the exogenous child were marked by a discontinuous and incoherent pattern as if the model was not being followed and attention was wandering from one part to another, the finished product appearing disorganized. The non-brain-injured child showed a more systematic procedure and followed the pattern of the model more closely. The importance which is given to test performance can be seen in Strauss' statement that "one or two incoherent placements on the marble board cannot be regarded as significant, but two or more incoherent moves on more than two patterns give strong indication of a disturbed visuomotor perception. . . ."

One question that arises about Strauss' criteria of brain injury concerns those cases in which positive neurologic evidence for brain injury is absent (see the definition quoted above). In such cases the diagnosis of brain injury is presumably based on psychologic test findings and behavioral observations. However, since the tests have been validated against neurologic data the former cannot be expected to be more discriminating than the latter. In addition the exogenous-endogenous test comparisons always revealed some overlap between the group so that in the absence of other data knowledge of test performance would seem to be an insecure basis for diagnosis. A similar situation would seem to obtain in regard to the diagnostic value of behavioral observations. Strauss points out that there is a good deal of behavioral similarity between the brain-injured and the child with psychopathic personality. In the absence of positive neurologic evidence, therefore, "exogenous behavior" does not allow one to make a diagnosis. In this connection Strauss states that even though neurologic evidence is lacking and measurable intellectual retardation is not present "whereas the behavior of the child in question resembles that characteristic for brain injury, and even though the performances of the child on our tests are not strongly indicative of brain injury, it may still be reasonable to consider a diagnosis of brain injury."

The last four chapters of the book are devoted to a statement of general principles in the education of the brain-injured child, the teaching of arithmetic fundamentals, and the teaching of reading and writing. The authors should be commended on their ingenuity in devising procedures which facilitate the learning process in these deviant cases. It is refreshing to see how the authors put into practice what too often is only preached, namely, that a careful analysis of a child's weaknesses and strengths must serve as the basis for what one does with *that* child. Rather than fit the child to the procedure Strauss and Lehtinen demonstrate how much can be gained by fitting the procedure to the needs of the child.

SEYMOUR SARASON

TECHNIQUE OF TREATMENT FOR THE CEREBRAL PALSY CHILD, Paula F. Egel, Introduction by Winthrop M. Phelps, M.D., Appendix by Moir P. Tanner, Drawings by Dorothea Mintline, The C. V. Mosby Company, St. Louis, 1948, $3.50, 203 pps., 49 figures.

This book is well written and printed, containing good illustrations. It deals with the technic of actual physical therapy of children with cerebral palsy. It discusses clearly and in detail many of the modalities employed. These include massage, passive motion, active and active associated motion, resistant motion, automatic and conditioned motion, relaxation, balance work, and some of the skills. There is also included a list of various types of equipment which can be employed for the cerebral palsied.

The first portion of the book deals with the medical aspects of cerebral palsy, and this is one of the weakest portions of the volume since it contains many inaccuracies. The book ends with an excellent chapter on the organization of cerebral palsy department in a children's hospital.

The book can be recommended for technicians dealing with children who are cerebral palsied. It would not be particularly valuable for parents since it is written from the technician's viewpoint. As a matter of fact there is very little mention of the aspects of parental training.

M. A. PERLSTEIN

PSYCHIATRIC RESEARCH, Cecil K. Drinker, Jordi Folch, Stanley Cobb, Herbert S. Gassner, Wilder Penfield, and Edward A. Strecker, Harvard University Monography No. 9 in Medicine and Public Health, Cambridge, Mass., Harvard University Press, 1947, 113 pp., 2 illustrations.

In this slight volume are reprinted six papers read at the dedication, on May 17, 1946, in Waverly, Massachusetts, of the Laboratory for Biochemical Research at the McLean Hospital, the mental disease department of the Massachusetts General Hospital. As the first in this series of addresses, Cecil K. Drinker contributes a dignified historical survey of past researches at the McLean Hospital, where, at the turn of the century, Otto Folin undertook a monumentally conceived but unfinished study of disorders of cerebral metabolism. In the direct line of descent from Folin as Director of Scientific Research, Jordi Folch sets forth a survey of brain function from the biochemical

point of view, a concise but comprehensive summary of present knowledge of normal cerebral metabolism, including an extensive bibliography. From this biochemical frame of reference, Stanley Cobb shifts the emphasis to the emotions and related disorders of bodily function in a discussion of the problems encountered in the integration of medical and psychiatric services at the Massachusetts General Hospital. In a brief summary of research findings, he cites some of the pioneering investigations carried on there in regard to the interaction of physiologic mechanisms in normal and disturbed emotional states, with a final, more exhaustive treatment of the syndrome known to cardiologists as neurocirculatory asthenia and to psychiatrists as the anxiety state. Dr. Cobb's emphasis on a pluralistic point of view towards etiology in this latter entity has particular pertinence for pediatricians who can exercise a preventive function of considerable importance.

One of the most unique contributions in this series is that of Herbert Gasser, Director of the Rockefeller Institute, who presents a plea for a thorough-going reexamination of psychiatric thought and communication from syntactical and semantic points of view. In sending forth this admirable call for heightened communicability, however, he betrays a neurophysiologist's understandable desire for expression of research data entirely in terms of physical and behavioristic concepts, a difficult goal in dealing with complex human emotions. The eminent neurosurgeon, Wilder Penfield, follows with a masterly discussion of "psychial seizures," a study in anatomic localization of psychic phenomena which has important implications for many medical disciplines. The final note is sounded in a psychobiologic key by Edward Strecker, a psychiatrist and teacher who reviews in a philosophic vein the present platform of departure for psychitatric research, indicating some of the similarities to and differences from the physical sciences which characterize investigations of the human psychobiologic unit.

If any criticism can be leveled at this well-balanced collection of facts and points of view, it derives from the weighted treatment of conscious mechanisms and objectively verifiable data to the virtual neglect of unconscious forces and motivations. Difficult as are these less obvious psychic phenomena to study quantitatively, they have at least empirical basis for existence, and certainly bear at least equal scrutiny with more readily quantifiable but less fundamentally motivating mechanisms.

DANGE G. PRUGH

RHEUMATIC FEVER, NURSING CARE IN PICTURES, Sabra S. Sadler, R.N., Philadelphia, J. R. Lippincott Company, $3.50, 144 pp.

This has been written primarily for parents to supplement the services of the public health or visiting nurse in the home of a family with a rheumatic fever patient. It shows through the text and through many photographs, the course of an 11 year old child with rheumatic fever; first in bed at rest, then the successive stages of recovery back to full activity, pointing out the physical, emotional, mental and social care needed at these stages. The photographs are excellent and illustrate the application of the written material in the text.

The text is divided into 8 chapters, first of which is a brief description of rheumatic fever, written by Reno R. Porter, M.D., of 12 pages; then in order—Understanding the Visit to Your Doctor—Preparation for Bed Rest—Personal Care of the Patient—Care Activities—Diet—Medications and Treatment—Home Teaching—Social and Emotional Factors in Rheumatic Fever—and Returning to Normal.

The book should serve its purpose well, that is, to supplement not to substitute services of the nurse visiting in the home. It should also serve the nurse well for her to use as an instruction book to be referred to by parents between visits, for better understanding of the nurse's directions and her care. All reading material of this type for parents is useful for special placement in the hands of those selected according to their ability to understand. It can be used as a supplement to the educational process. The book is well prepared and sound in principle. The author is well qualified by her training, experience and interest to deal with the subject, and it is fortunate that she has taken the time to go about writing the book. The book should be in the hands of every professional worker in this field and with only a few limitations in the hands of those parents for whom it was intended.

HUGH MCCULLOCH